Introduction to Neonatology

Preface

Neonatology is a sub-specialty of pediatrics that focuses on conditions that affect babies at the time of birth, especially babies born prematurely. Unlike pediatrics, which primarily deals with the growth and development of normal children, neonatology focuses on sick babies, particularly premature babies that are physiologically unprepared for life outside the womb. In addition, neonatology deals with full-term babies that are born with problems such as infections or birth trauma. Another difference from pediatrics is that neonatology deals exclusively with babies in hospitals. There is no such thing as outpatient neonatology.

Chapter one covers the history of neonatology. You will learn that neonatology is a relatively new specialty. We will discuss where neonatology first appeared as a subspecialty. Who the first neonatologists were – they were not pediatricians – and when neonatology become a pediatric sub-specialty. We also discuss the intersection between medicine and technology as it relates to neonatology and how advances in technology made neonatology possible for the care of extremely low birthweight babies. Finally, we will discuss the epidemiology of neonatology: how many premature and sick babies are born in the United States annually, and how many neonatal intensive care units – or N.I.C.U.'s (pronounced "nick-yous") – are there.

Chapter two provides an overview of perinatal medicine. Perinatal medicine means the science and care of babies surrounding the moment of birth. This includes the period while they are still in the womb. The care of pregnant mothers is a concern for the neonatologist, though the mothers are actually cared for by obstetrician/gynecologists. There are several medical

conditions in pregnant women that may impact the health of their fetus and will be important when the baby is born. These include medical conditions and the effects of drugs the woman may be taking. We will briefly discuss the emerging field of fetal medicine, including advanced prenatal surgery.

Chapter three is devoted to the process of birth – the delivery of a baby. The way a baby adapts to living outside the womb is a particular concern of neonatology, as the process sometimes goes awry. We will discuss the effects of the birth process on the neonate, as well as particular conditions and injuries that may occur at the time of birth. Finally, we touch on the process of transporting a sick newborn to a hospital that has a NICU.

In chapter four, we will discuss the normal newborn infant. This chapter covers the routine physical examination of the newborn, feeding, and common normal problems that occur during the first days of life. Finally, we will briefly discuss support for mothers and other caregivers, an issue that becomes especially important when we discuss sick newborns in the NICU.

Chapter five is devoted to the sick newborn. We talk about admission to the NICU and issues specifically related to stabilization of a sick newborn. Since premature infants have very specific developmental needs, we will cover some issues related to developmental care of sick newborns.

In chapter six, the focus is on the problems that are unique to the premature infant. We will discuss the premature lung and the problems that occur when a baby is born with underdeveloped lungs. Most people associate premature babies with incubators. We will explain

why incubators are necessary for premature babies. We will talk about special considerations regarding nutrition and growth in newborns, and how these problems are handled in the NICU. There are specific problems that might occur in premature brains, eyes, hearts and bones. There are also infections that are unique to newborns that are important to understand. Finally, chapter six talks about outcomes for premature infants – what is life like for a "NICU graduate".

Chapter seven deals with neonatal problems in full-term babies. There are a number of infections that newborns are susceptible to. These infections are different from infections that older children are susceptible to. We discuss problems related to the brain and respiratory system that are different from the problems experienced by premature babies. There are issues related to the control of blood glucose and other metabolic problems. We discuss congenital abnormalities of the nervous system, the heart, the gastrointestinal tract, the kidneys, the skin, and the sexual organs. There are issues related to bones and muscles of newborns. Finally, chapter seven deals with blood problems in newborns.

Chapter eight is dedicated to the neonatal intensive care unit. The NICU is very different from other in the hospital. We will deal with issues related to pain management, dosing medicines in neonates, and how NICUs are always attempting to improve quality. Since NICUs and neonatologists tend to be located in academic institutions, we cover issues related to research, especially ethics and parental consent. The special case of the dying neonate is also covered. Finally, we deal with the happier subjects of hospital discharge and follow-up.

Chapter one: History and epidemiology

Though today virtually all neonatologists are pediatricians, this was not the case in the early history of neonatologists. The first neonatologists, in the 1900s, were obstetricians, midwives and anesthesiologists. This was the period of specialization and increasing numbers of births were taking place in hospitals. The first professionals to see and take care of newborns were midwives and obstetricians. Obstetricians also managed any known medical problems that a pregnant woman might have.

The history of medicine owes a great debt of gratitude to obstetrics for helping to reduce infant deaths. In the mid-nineteenth century, no one knew that bacteria were responsible for the infections that killed mothers and babies in maternity wards. Ignaz Semmelweiss, a Hungarian obstetrician, discovered that washing one's hands before examining a mother drastically reduced the risk of mothers and babies dying (Figure One). It turned out that doctors would attend to mothers after having performed autopsies, after which mothers and their babies occasionally died of febrile diseases. However, the mothers attended by midwives tended not to develop fevers or die. Semmelweiss figured out that the midwives' clean hands must have something to do with it. He did not know why hand washing worked, because the germ theory of disease was not yet widely accepted.

Meanwhile, in France, obstetricians were busy trying to figure out how best to care for babies born early. French obstetricians were the first to experiment with tube feeding of babies that were too immature to feed on their own. The first infant incubators were also developed in France.

Biographical sketch: Madame Henry, the first neonatologist

The history of modern neonatology began in France in the 1880s. Shortly after the experimental introduction of the incubator, a special wing of the maternity ward was established by Dr. Stephane Tarnier, the obstetrician-in-chief at the University of Paris (Figure Two). Dr. Tarnier appointed "Madame Henry" (history has lost her given name) to run the first special care nursery.

Madame Henry's charge was to experiment with ways to improve the hospital's atrocious infant mortality statistics. Among her most important tools were six incubators and five wet nurses. According to reports, ninety percent of the patients on the ward were breastfed. Of the patients who died, it was noted that congenital malformations accounted for the majority. Even today, congenital malformations are a major cause of infant mortality. Of the infants who were formula fed, astonishingly high numbers died of intestinal infections. Although experiments in boiling milk before feeding were performed, we have no records regarding the results of such experiments. It was well understood, however, that breastfed babies had better survival rates than formula-fed babies.

Madame Henry resigned her post one and a half years later, when another luminary in the history of neonatology, Dr. Pierre-Constant Budin, took the position as obstetrician-in-chief.

Incubators were introduced to the United States in a rather unusual manner. In the early twentieth century, hospitals did not allow equipment such as incubators. So, students of the French obstetricians began to display infants in incubators at public fairs, such as the 1933 World's Fair

in New York. In our current era of patient privacy, it is difficult to imagine displaying newborns in public exhibitions, but at the time, so-called “side-show babies” led to the adoption of incubators in the major hospitals across the United States.

The modern history of neonatology in the United States began after World War II, when hospitals began to set up special care units specifically for sick newborns. These were the precursors to the modern NICUs.

By this time, the germ theory of disease was well accepted and antibiotics had been invented. However, there was little knowledge as to how newborn babies contracted infections and became sick. After World War II, special care units for babies began paying special attention to hygiene and infection control. This made a huge difference in terms of reducing neonatal infections.

It was not until the 1970s that premature babies began to be treated with mechanical ventilation and other technologies. Perhaps the greatest advance in the history of neonatology was the development of surfactant replacement therapy in 1980. The role of surfactant and replacement therapy will be discussed in detail in chapter six.

There is a substantial need for neonatologists and NICUs in the United States. Approximately twelve-point-five percent of newborns are born prematurely, meaning before thirty-seven weeks’ gestation. This accounts for over seventy-five percent of the infant mortality in the US.

About half of preterm births occur for no known reason. One third occur because of premature rupture of membranes. The remaining premature births occur because of medical problems in the mother or because the birth was induced electively.

According to the World Health Organization, Southern Africa has the highest incidence of preterm birth, at almost eighteen percent. The lowest incidence occurs in Central Asia, at about four percent. International comparisons are difficult to make, as are estimates of the infant mortality rate, because the definition of a live birth varies from country to country. Despite the lack of accuracy, it is clear that prematurity is a major contributor to the infant mortality rate, and premature birth is a substantial problem worldwide.

Key Takeaways

- Neonatology is a medical specialty focused on newborns, especially premature newborns
- The first neonatologists were obstetricians
- France produced the first tube feeding devices and incubators
- The major turning point in the history of neonatology was the invention of surfactant replacement therapy in 1989

Quiz

1. Which patients are the concern of neonatologists?
    a. Fetuses
    b. Pregnant mothers
    c. Newborn babies
    d. all of the above

Answer: d. Neonatology is a branch of pediatrics that deals with newborn babies, including prior to birth, which makes pregnant mothers an object of study as well.

2. In what century did neonatology emerge as a distinct specialty
    a. Seventeenth
    b. Eighteenth
    c. Nineteenth
    d. Twentieth

Answer: c. The first doctors to treat sick newborns did so in the mid to late 1800s (the nineteenth century)

3. Who discovered that handwashing saved baby's and mothers' lives?
    a. Ignaz Semmelweiss
    b. Louis Pasteur
    c. Alexander Fleming
    d. Mary Ellen Avery

Answer: a. Louis Pasteur is credited with establishing the germ theory of disease. Alexander Fleming discovered penicillin. Mary Ellen Avery discovered surfactant replacement therapy

4. In the US, what percentage of deliveries are pre-term?
    a. Five percent
    b. Ten percent
    c. Twelve-point five percent
    d. Seventeen-point eight percent

Answer c. According to the WHO, the US has an approximately twelve-point five percent premature birth rate, meaning less than thirty-seven weeks' gestation.

5. What is the leading cause of the infant mortality rate?
    a. Congenital abnormalities
    b. Preterm birth
    c. Neonatal infections
    d. SIDS

Answer b. Premature birth, especially of extremely low birthweight infants, is the leading cause of infant mortality in the United States.

Chapter two: Perinatal medicine

Pre-pregnancy care

Care of the newborn begins before birth. Mothers who do not seek prenatal care are at increased risk for many complications, including preterm birth. The reasons that mothers do not seek prenatal care in the US are complex including problems with alcohol and substance abuse. Others avoid prenatal care for psychological reasons, including denial. For some mothers, the financial burden of prenatal care is too high. Finally, a small portion of mothers who do not seek prenatal care do not believe that they need to do so.

Because failure to seek prenatal care is so closely tied to alcohol and substance abuse, babies born to these mothers suffer from low birth weight, drug addiction, and neonatal infections. We will discuss these problems separately in future chapters.

Prenatal care involves regular check-ups with an obstetrician. These become more regular as the due date approaches. The mother is screened for a number of infectious diseases. We will discuss these in more detail in the next section. The mother's weight and blood pressure are measured. Urine tests are also frequently performed. Her blood sugar is also measured. These exams and tests are performed to ensure the mother is not experiencing any side effects of pregnancy such as pregnancy-induced hypertension or gestational diabetes.

At prenatal visits, the fetus is examined by ultrasound to ensure that it is growing at the expected rate. If there are any abnormalities noted on ultrasound, these are followed-up closely. Sometimes the follow-up involves only more frequent ultrasounds exams. Other times the mother is referred for genetic testing or amniocentesis.

If the mother or the fetus has any problem that requires further follow-up, she is often referred to a high-risk pregnancy specialist. High-risk pregnancies are more likely to result in preterm birth and involve a congenital malformation found on ultrasound. Sometimes, mothers are considered high-risk for being in an older age group. Advanced maternal age is defined as thirty-five years or older.

Prenatal screening

Prenatal blood tests include a number of tests for infectious diseases. These include

- HIV and other sexually transmitted diseases
- Anemia
- Diabetes

- Hepatitis B
- Measles, mumps, and rubella

Mother's cervix is also checked for a bacterium called Group B strep. This is the most common cause of neonatal sepsis. In addition, a Pap smear is performed to screen for cervical cancer. If the mother is not immune to measles, mumps, or rubella, the doctor will recommend the mother be immunized. This is because congenital rubella is associated with several birth defects.

Special screening tests generally only performed on pregnant women include:

- Human chorionic gonadotropin – a measurement of the progress of the pregnancy.
- Alpha fetoprotein – a screening test for the presence of neural tube defects.

We will discuss neural tube defects in a later chapter. Alpha fetoprotein is also used to screen for the possibility that the infant might have genetic abnormalities such as Down syndrome. If the levels of alpha fetoprotein are elevated beyond a certain range, the mother is usually referred for further tests. These are usually amniocentesis or chorionic villus sampling to check for the presence of Down syndrome in the fetus.

The nonstress test

The nonstress test is completely passive (Figure Three) and nothing is done to stress the fetus. The object of the test is to screen for the general well-being of the fetus and the progress of the pregnancy. Nonstress tests are performed beginning in week twenty of gestation. A fetal heart rate monitor is placed on the mother's abdomen for as long as twenty minutes. It is expected that there will be a fair number of accelerations of the fetal heart rate during that time, indicating that the fetus is active. Two or more accelerations indicates a reactive, or positive test. A non-reactive

test is when there are fewer than two accelerations over a forty-minute period. A non-reactive test indicates need for a secondary screen, often a biophysical profile.

Biophysical profile

The biophysical profile consists of several parts, including ultrasound (Figure Four). The following five parameters are included in the profile: fetal heart rate, breathing movements, body movements, muscle tone, and quantity of amniotic fluid. Each parameter is rated on a scale from zero to two. In this regard, the biophysical profile resembles the Apgar score that is described in a later chapter.

Biophysical profile scores of eight to ten are considered reassuring. A score of six is considered borderline. In cases of equivocal results, the biophysical profile is repeated, usually in one to two days. If the baby is at term, an equivocal score may be an indication for delivery. If the score is four or less, further testing is often done, or if the baby is close to term, urgent delivery is indicated. Regardless of the score, a paucity of amniotic fluid is considered a red flag. Low fluid levels trigger more frequent testing or a decision to go forward with induction of labor.

Contraction stress test

As the delivery date approaches, prenatal care visits may include a contraction stress test (Figure Five). The test is designed to evaluate the fetus's responses to uterine contractions. This test resembles the non-stress test in that it includes fetal heart monitoring. In addition, contraction monitors are placed and the two tracings are compared.

Because of compression during contractions, oxygenation of the fetus should become transiently decreased. This may result in decreases in fetal heart rate. If the decelerations occur late in the contraction cycle, studies have shown a correlation with increased neonatal depression and fetal demise. Depending on the state of the fetus's gestation, late decelerations are an indication for emergent cesarean section.

If the obstetrician team and the mother agree that there is sufficient time, the maturation of the fetus's lungs will be measured prior to delivery. This test is performed via amniocentesis. The withdrawn amniotic fluid is subjected to thin layer chromatography. The test is looking for a ratio of lecithin to sphingomyelin. A ratio of more than two point four suggests that the infant's lungs are producing adequate surfactant. In other words, the risk of respiratory distress syndrome will be lower. Respiratory distress syndrome will be discussed in more depth in chapter six, when we discuss problems particular to the premature infant.

If the lecithin to sphingomyelin is less than two point five, and the fetus is not distressed, a decision may be made to accelerate fetal lung maturation. This is accomplished via administration of the steroid betamethasone to the mother. Administration of the steroid rapidly accelerates fetal lung production of surfactant. The treatment is effective but not perfect. A small of betamethasone-complete newborns will nevertheless develop respiratory distress syndrome shortly after birth.

Fetal medicine

This is a relatively new branch of medicine. Until recently, it has not been possible to treat fetuses before they are born. However, advances in technology, particularly imaging techniques, have made treatment of prenatal problems a possibility. Here are a few examples:

- Prenatal blood transfusion – there are some medical conditions that cause babies to become very anemic. Some of these conditions can be fatal to the fetus, resulting in stillbirth. Today, these conditions can be treated with prenatal blood transfusion. New ultrasound technology makes it possible to access the blood vessels in the baby's umbilical cord. A needle wide enough to transfuse whole blood is then inserted.
- Ureteropelvic junction repair – a rare congenital anomaly of the kidneys occurs when the ureter becomes blocked on one side. Left untreated, the back pressure from urine produced by the kidney can result in loss of function on the affected side. Since hydronephrotic kidneys (swollen) are easy to see on ultrasound, the condition can be diagnosed. These obstructions can be fixed by directly on the fetus by opening the uterus, as in a cesarean section. Then the fetus is operated on and replaced in the uterus to finish gestation.
- Congenital diaphragmatic hernia – this entity will be discussed in considerable detail in chapter seven. For now, it is sufficient to know that this is an example of a procedure that can reduce the pulmonary hypoplasia that often accompanies congenital diaphragmatic hernia.
- Congenital cystic adenomatoid malformation – this entity will be discussed among related congenital malformations of the lung in chapter seven. For now, it is important to realize that the reason for removal of these lesions early is prevention of newborn respiratory distress.

- Several types of fetal congenital heart disease are amenable to fetal surgery. This is because some varieties of congenital heart disease already develop complications by the time the infant is born. For example, the tetralogy of Fallot includes right ventricular hypertrophy. This hypertrophy might be substantially reduced if the defects could be partially corrected in utero.
- Sacrococcygeal teratoma – By definition, these are primitive cell tumors originating in the base of the spine. Because they have a tendency of malignant transformation, these teratomas are often removed in utero.
- Spina bifida. This is a neural tube defect that will be discussed in more detail in chapter seven. Spina bifida is one congenital malformation that can now be treated with prenatal minimally invasive surgery. Such procedures can be performed through a device called a fetoscope. Minimally invasive surgery of this type can be safer with equivalent efficacy to open abdominal procedures.

As the technology advances, we can expect that the range of congenital anomalies fixable by prenatal surgery will expand.

Maternal medical conditions

A number of medical conditions in the mother bear directly on the condition of the fetus. These will be presented in terms of organ systems of the mother: endocrine, hematological oncological, infectious, neurological, and finally cardiac.

Maternal endocrine conditions

The most common endocrine disorder affecting pregnant mothers is gestational diabetes mellitus. This is defined as high blood sugar after the oral glucose tolerance test. The mother drinks a sugar-containing drink and her blood sugar is measured at various intervals afterward. The causes of gestational diabetes are not completely understood. However, a substantial number of mothers with gestational diabetes mellitus develop type two diabetes later in life. Therefore, is possible that the metabolic stress of pregnancy causes the woman to develop diabetes years before she would otherwise develop the disease. However, this does not explain the substantial number of women with gestational diabetes who never develop diabetes later in life.

High blood sugar is a problem for the developing fetus. Even though the mother's pancreas may not be producing enough insulin to properly control her blood sugar, the fetus's pancreas works perfectly well. As a result of excessive sugar entering the fetal circulation from the placenta causing the fetus to grow faster than normal. As a result, the fetus may grow too large to be delivered vaginally. Infants of diabetic mothers will be discussed in more detail in chapter seven.

Next most common among endocrine disorders affecting pregnant mothers are problems related to the thyroid, either hyperthyroidism or hypothyroidism. The most common cause of hyperthyroidism in pregnancy is Graves' disease. The most common cause of hypothyroidism in pregnancy is Hashimoto's thyroiditis.

Graves' disease is the most common cause of neonatal hyperthyroidism. In adults, the other name for the disorder is diffuse toxic goiter. It is an autoimmune disorder, caused by the action

of an endogenous antibody called the thyroid stimulating immunoglobulin. The antibody interacts with cells in the thyroid in a similar fashion to that of thyroid stimulating hormone.

The result is that mothers and their newborns develop signs and symptoms consistent with elevated thyroid hormone levels. The diagnosis may be suspected based on symptoms and confirmed with blood tests and radioiodine uptake. In the mothers, the symptoms include irritability, weakness, poor sleep, tachycardia, heat intolerance, diarrhea, and unintentional weight loss. The latter is clearly a problem for a pregnant woman. These same symptoms may be present in the newborn.

The therapy of Graves' disease in the newborn is supportive. Because the symptoms are caused by transplacental movement of the thyroid stimulating antibodies, the latter will be cleared by the baby's own system in days to weeks.

Hashimoto's thyroiditis is also an autoimmune disease. By contrast to Graves' disease, which causes hyperthyroidism, Hashimoto's thyroiditis gives rise to hypothyroidism. The autoimmune process destroys the mother's thyroid with lymphocytic infiltrates. For this reason, the disease is also known as chronic lymphocytic thyroiditis. The familiar symptoms of hypothyroidism include weight gain, fatigue, constipation, and depression.

Like Graves' disease, Hashimoto's thyroiditis is associated with the development of anti-thyroid antibodies. However, unlike Graves' disease, the antibodies associated with Hashimoto's thyroiditis at most cause a transient hypothyroidism in the neonate. The most severe

consequences to the developing fetus and neonate result from the deficiency of circulating thyroid hormone in the mother, as we will discuss.

Complications of untreated hyperthyroidism in pregnancy include:

- Spontaneous abortion
- Preterm labor
- Low birth-weight
- Stillbirths
- Hypertension

Untreated hypothyroidism can cause:

- Preterm birth
- Low birth weight
- Respiratory distress

Note that both hyperthyroidism and hypothyroidism can cause preterm births and low birthweights. Therefore, it is essential to ensure that pregnant mother's thyroid functions are within normal limits.

Maternal hematologic oncological conditions

A number coagulation disorders in pregnant women have important implications for their fetus. Of these, two coagulation disorders have significant impact on fetuses, Factor Five Leiden and the antiphospholipid syndrome. Factor Five Leiden is a coagulation disorder that causes thromboses, or clots, to form in the blood vessels of the placenta. This is a clotting disorder that can cause blood clots to form in the blood vessels in the placenta during pregnancy. This can be

fatal to the fetus. Antiphospholipid syndrome affects up to five percent of women during pregnancy. This is an autoimmune disorder. In addition to causing miscarriages, antiphospholipid syndrome can cause preeclampsia, a condition we will discuss later on, preterm labor, and intrauterine growth restriction, which we will talk about after the maternal medical conditions section.

Recall that this section was called hematologic oncological conditions. Oncology is mentioned because some pregnant women do indeed have cancer. Cancer is not necessarily fatal to the mother or the fetus. In fact, there are many women who successfully deliver healthy babies while taking chemotherapeutic agents. Most chemotherapeutic agents work by preventing cells from dividing. If this is so, it is reasonable to ask how a growing fetus can survive exposure to these drugs. The answer is that these medications are discontinued during the first trimester, when fetal organs form. The same goes for radiation treatments. It turns out that a woman with cancer and her fetus can survive fairly well if cancer treatment is carried out during the second and third trimesters, only.

Maternal neurological conditions

If a mother has a seizure disorder, she and her doctors need to be careful as to what seizure medicine she takes. Valproic acid has been associated with a number of congenital abnormalities. The most common of these is the neural tube defect, spina bifida. We will discuss spina bifida in chapter seven.

The other important maternal neurological condition to be aware of is myasthenia gravis. This is an autoimmune disease in which the immune system generates antibodies against the neuromuscular junction. This results in muscular weakness or paralysis. The problem for newborns is that maternal antibodies can cross the placenta. In neonates, these antibodies can cause complications ranging from mild hypotonia to respiratory distress. The condition is transient, as the antibodies are eventually cleared.

Maternal cardiovascular conditions

The most important maternal cardiovascular condition to be aware of is preeclampsia. Preeclampsia is a complex condition characterized most prominently by high blood pressure.

Preeclampsia

Preeclampsia is a disorder of the function of vascular endothelial cells. It is also characterized by diffuse vasospasm, as we will discuss shortly. It most often begins after twenty weeks of gestation. Preeclampsia can also occur up to one month after the baby is delivered. Clinical signs include high blood pressure and protein in the urine, or proteinuria. Sometimes mothers with preeclampsia present with lower extremity edema.

Preeclampsia is named as such because of its relationship with its more severe manifestation, namely eclampsia. Eclampsia is characterized by seizures and the syndrome called HELLP. The acronym stands for hemolysis, elevated liver enzyme, and low platelets.

For the fetus, the most effective treatment for preeclampsia is delivery. Therefore, preeclampsia is a very common reason for preterm birth. Obstetricians attempt to control maternal blood pressure adequately until the fetus is mature enough to be delivered safely.

Symptoms in the mother and the fetus that are indications for urgent cesarean section include non-reassuring fetal monitoring. The expression non-reassuring means a poor result on the non-stress test, and a poor biophysical profile score. In addition, the obstetrician will perform Doppler ultrasound looking at the direction of flow in the umbilical artery. If it is reversed on diastole, this is an indication for delivery. Ruptured membranes are another indication for immediate induction or cesarean section.

If the mother's blood pressure cannot be controlled with medical therapy, the fetus must be delivered. For many years, the salt magnesium sulfate was used to lower maternal blood pressure. The practice was abandoned when meta-analyses revealed that outcomes were not improved with magnesium sulfate, and in fact more harm than good came of the therapy. Studies such as these will be mentioned again in chapter eight when we discuss evidence-based medicine.

There are two other fetal-related complications of preeclampsia that constitute indications for immediate delivery of the fetus. One is oligohydramnios, or low amniotic fluid levels. The other is severe intrauterine growth restriction to less than five percent of predicted.

Intrauterine growth restriction

By definition, an infant with intrauterine growth restriction is born with a weight less than ten percent of what is predicted for gestational age. There are two types of intrauterine growth restriction: asymmetric and symmetric. Asymmetric is more common. Because the developing brain receives nutrition preferentially, in conditions of placental deprivation, the brain is relatively spared. Therefore, the growth restriction of the brain tends to be less than that of the body. Occasionally, the head has normal size in the context of a low birth weight baby. In the rarer symmetric intrauterine growth restriction, the head and the body are proportionally small.

The most common causes of symmetric intrauterine growth restriction are:

- Early infections, such as cytomegalovirus and rubella
- Chromosomal abnormalities
- Anemia
- Maternal drug use

There are three classes of asymmetric intrauterine growth restriction, based on the source of the problem: maternal, placental, and fetal.

The most common maternal causes of asymmetric intrauterine growth restriction are:

- Low pre-pregnancy weight
- Poor nutrition and weight gain before and during pregnancy
- Anemia
- Alcohol and/or drug use

- Smoking
- Recent pregnancy
- Gestational diabetes. When severe, vessels in the placenta can suffer from the same types of problems that occur in other diabetic end-organ complications. Keep in mind that milder forms of gestational diabetes cause fetal macrosomia, or excessive growth, as opposed to growth restriction.
- Pulmonary disease
- Cardiovascular disease. Both this category and pulmonary disease lead to the same common endpoint, that is inefficient delivery of oxygenated blood to the placenta
- Renal disease
- High blood pressure
- Celiac disease and other malabsorption syndromes

The most common placental causes of intrauterine growth restriction are:

- Preeclampsia, probably because of constriction of placental vessels
- Multiple gestation, most often related to twin to twin transfusion syndrome
- Uterine malformations that limit the extent of fetal growth
- Placental insufficiency, which has many subclasses, including some already mentioned briefly. Some more detailed descriptions of placental pathology will be our next topic.

Placental insufficiency

Placental insufficiency is defined primarily by its results. When the fetus fails to grow properly because of failure of the placenta to deliver nutrients, by definition the placenta is insufficient. Placental insufficiency can be broadly divided into two categories. Either the placenta fails to form correctly or it becomes damaged.

The causes of placental insufficiency are not completely understood. However, there are a number of placental features that have been associated with insufficiency. The problem with these classifications is that the following conditions may also be present in placentas with normal function:

- Thin placenta of less than one centimeter.
- Circumvallate placenta, seen in one percent of normal placentas.
- Amnion cell metaplasia, that is also seen in the majority of normal placentas.
- Large numbers of syncytial knots
- Placental calcifications
- Placental infarcts with blood vessel thickening

In addition to intrauterine growth restriction, the effects on the fetus of placental insufficiency include the following: oligohydramnios and its sequelae, preeclampsia (as discussed recently), miscarriage and stillbirth.

One result of chronic fetal hypoxia from placental insufficiency is that the fetal bone marrow will attempt to compensate. Hypoxia leads to increased production of erythropoietin by the kidney. The bone marrow responds to erythropoietin by making more red blood cells to increase

oxygen carrying capacity. The result may be perinatal polycythemia. Thickened blood is more prone to thrombosis and thrombotic consequence including organ damage.

A poorly-functioning placenta also fails to deliver adequate amounts of maternal immunoglobulins to the fetus. As a result, the newborn is more susceptible to infections than is the product of a normally-functioning placenta.

Decreased umbilical vein blood flow also has deleterious consequences. Decreased flow through the umbilical vein results in a compensatory reaction in which more umbilical vein blood is diverted to the fetal heart. Over time, the cumulative effect of increased pulmonary vascular resistance leads to decreased fetal cardiac output, and eventual fetal demise.

There are behavioral consequences of placental insufficiency as well. Hypoxic fetal brains are subject to decreased central nervous system maturation. Fetuses with insufficient placentas show less activity than normal fetuses.

Finally, placental insufficiency may give rise to later metabolic changes in the child or young adult. The so-called thrifty phenotype theory suggests that fetuses exposed to chronic low-level hypoxia undergo epigenetic changes. These changes result in compensatory metabolic fine-tuning that predisposes the infant to developing obesity and type two diabetes later in life.

The most common fetal causes of intrauterine growth restriction are chromosomal abnormalities and viral infections passed through the placenta, particularly cytomegalovirus.

Multiple gestation

The most common multiple gestation is fraternal, or non-identical twins. This occurs about once in every eighty pregnancies. It is more common with advanced maternal age. The general demographic trend of older mothers, combined with the use of assistive reproductive technologies, has given rise to an increase in multiple gestations over time. Multiple gestations of more than triplets are exceedingly rare without the use of assistive reproductive technologies.

The most common complication of multiple gestation is preterm delivery. The normal human uterus evolved to develop one fetus at a time. Nevertheless, there are numerous reports of almost normal sized twins born almost at term. For higher multiples, prematurity and low birth weight are much more common. For similar reasons, the rate of cesarean delivery is markedly higher for multiple gestations than for singletons.

In addition to prematurity and low birth weight in multiple gestations, there is a somewhat higher incidence of hypoxic ischemic injuries, leading to a higher incidence of cerebral palsy among multiples than in the singleton population.

Preterm delivery

A delivery prior to the beginning of the thirty-seventh week of gestation is considered premature. Although the causes of preterm delivery are not completely known, the best-known risk factors are:

- Diabetes

- Hypertension
- Multiple gestation
- Obesity or underweight
- Vaginal infections
- Smoking

Preterm birth is the leading cause of neonatal mortality. Neonatal mortality is distinct from infant mortality. Infant mortality refers to death during the first year of life. Preterm birth is responsible for 25% of the neonatal mortality rate.

The specific complications of preterm birth will be discussed in detail in chapter six.

A number of interventions have been developed to attempt to forestall preterm delivery. If prevention is not possible, obstetricians try to prepare the baby's lungs for birth. The process of interrupting or slowing labor is called tocolysis. This is accomplished by admitting the mother to the hospital and treating her with agents designed to reduce or stop uterine contractions. These include calcium channel blockers and beta agonists. Tocolysis rarely delays delivery more than two days. However, this length of time is adequate to treat the mother with the steroid betamethasone. This has been shown to rapidly accelerate the development of the fetus's lungs, so that it may be better able to breathe air.

Congenital and genetic disorders

There are two types of congenital disorder. The first kind are structural birth defects, when a part of the body develops incorrectly. The second are functional birth defects, when a particular body part does not work correctly. Many congenital disorders involve a combination of the structural and functional defects. Congenital disorders may be genetic in origin or may occur as a result of intrauterine infection or exposure to a toxic agent. The toxic agents causing congenital disorders are called teratogens. There is also one special class of congenital disorders that is caused by a vitamin deficiency. The congenital disorders are neural tube defects, and the vitamin is folate, also called folic acid or vitamin B-9. This particular disorder has been markedly reduced by the widespread use of prenatal vitamins containing folate.

There are four subclasses of congenital malformation:

- *Malformations* are disorders of tissue development. They most often occur during the first trimester. Cardiac defects such as the tetralogy of Fallot for example.
- *Dysplasias* are disorders at the organ level. They are caused by problems with tissue development. Brain abnormalities such as agenesis of the corpus callosum for example.
- *Deformations* arise from mechanical stress to normal tissue. Deformations often occur in the second or third trimester and can be due to oligohydramnios. Examples are intrauterine finger amputations.
- *Disruptions* are breakdowns of normal tissue. Maternal infections affecting brain development for example.

When a number of these congenital disorders occur in order, it is referred to a sequence. When they happen simultaneously, or there is no known order, it is called a syndrome.

Genetic disorders underlie most congenital anomalies that are not known to have been caused by infections or toxic exposures. As the human genome is vast, there are numerous locations where alterations in the genetic code can give rise to disordered development. The best known of these is Down syndrome (Figure Six). Note that there is no apostrophe S attached to the word Down. Down syndrome is also called trisomy twenty-one, because affected individuals have an extra copy of chromosome twenty-one. It is called a syndrome because it involves a number of parts of the body, including the brain, the face, and the musculoskeletal system, among others.

Maternal drugs affecting the fetus and newborn

Several agents that a mother ingests can have adverse effects on the fetus or newborn. Not all of these are drugs of abuse. In chapter four, we will discuss in more detail with drugs of abuse. In this section, we will discuss medications and legal substances that nevertheless have deleterious effects on the fetus and newborn.

Cigarettes and alcohol

Tobacco products and alcohol deserve brief mention here, as they are legal substances that adversely affect the fetus. Several substances in cigarette smoke have adverse effects on function of the placenta, causing it to function improperly. As a result, cigarette smoking is associated with low birth weight. Fetal alcohol syndrome is characterized by recognizable facial features. However, the greatest concern for maternal alcohol consumption is its effect on the development of the fetal brain. As with many organs, the first trimester is the most sensitive period of development for the brain. Excessive alcohol intake has been associated with delayed

neurobehavioral and cognitive development. As with many other toxic exposures, alcohol exposure is associated with preterm birth and low birth weight.

Medications

The following is a list of medications that are contraindicated in pregnancy, as they are considered teratogens. That is to say maternal ingestion of these medications can lead to congenital abnormalities. This list is by no means exhaustive. Women who are pregnant or are considering becoming pregnant any medication should consult their physician before taking any medication.

- ACE (angiotensin converting enzyme) inhibitors, taken to control blood pressure
- Angiotensin II antagonists, also for blood pressure
- Isotretinoin, an acne drug
- High doses of vitamin A
- Lithium, a mood stabilizer
- Male hormones
- Some anticonvulsant medications, especially valproic acid
- Anti-metabolic chemotherapeutic agents
- Antimetabolites, such as methotrexate
- Some thyroid medications
- Thalidomide, originally marketed as a mild sedative, now indicated for skin disorders
- Warfarin, a blood thinner
- The hormone diethylstilbestrol (DES), once given as a medication for morning sickness

Congenital infections

A number of bacterial and viral infections can affect a mother during pregnancy. The most important bacterial infection to remember is Group B Strep. There are also several important viruses that will be discussed in more detail.

Group B strep, as its name implies, is a Streptococcus that colonizes the cervix, vagina, and rectum of between fifteen and thirty-five percent of all pregnant women. Yet it causes problems for newborns in only about one in one thousand births. Mothers who test positive for Group B Strep during pregnancy are usually treated with antibiotics during labor. This drastically reduces the chances of passing the bacterium to the newborn. If left untreated, the organism is the most common cause of neonatal sepsis, including delayed neonatal sepsis. We will deal with the care of the newborn exposed to Group B Strep in a later section.

Syphilis is a special case, because syphilis is a spirochete (SPY-ro-keet), which is neither a bacterium nor a virus. Nevertheless, congenital syphilis is a serious condition, leading to birth defects and failure to thrive. This sexually transmitted disease is easily treated with antibiotics.

Urinary tract infections

Pregnant mothers frequently experience urinary tract infections. These infections are common and pose risks to both mother and fetus. Pregnancy is associated with physiological changes, as well as changes in structural relationships in the female urinary tract. These all give rise to an increased risk for ascending urinary tract infections. It is common practice in prenatal screening,

as describe in chapter two, to perform urinalysis. All bacteria detected in the urine are treated as urinary tract infections. This is even if the mother has no symptoms. The reason is that pregnant mothers are at higher risk for pyelonephritis.

The problem with treatment of urinary tract infections in pregnancy is that a number of antibiotics are known or suspected teratogens. Nitrofurantoin and trimethoprim-sulfamethoxazole are relatively contraindicated in the first trimester because of an association with neural tube defects. By contrast, these two antibiotics are the antibiotics of choice for urinary tract infections in the second and third trimester.

Fluoroquinolones are contraindicated throughout pregnancy because of animal studies showing teratogenic effects. Aminoglycosides such as gentamicin are contraindicated because they are known to be nephrotoxic. The fear is that these antibiotics may damage the fetal kidney.

When choosing an antibiotic for a pregnant woman, it is best to consult a manual containing classifications of known or suspected dangers to the fetus. In cases of doubt, it is preferable to err on the side of safety.

Viral infections

A number of viruses cause problems for newborns. Most of these viral infections are screened for and treated during pregnancy, but some are not.

- **Hepatitis B and C**. The management of babies born to hepatitis B positive mothers will be discussed in chapter four.
- **Human immunodeficiency virus, HIV**. This is usually screened for in prenatal care. If a mother is positive for the human immunodeficiency virus, there is a protocol of treatment for mother and baby that has drastically reduced maternal newborn transmission of HIV.
- **Cytomegalovirus, CMV**. Cytomegalovirus complicates about one percent of all live births. Fetuses exposed to CMV are prone to develop numerous neurological problems, particularly mental retardation and sensorineural hearing loss. Although there are some antiviral protocols for treating mothers and babies, often the recommendation for cytomegalovirus positive mothers is to consider pregnancy termination.
- **Herpes simplex virus, HSV**. Herpes simplex virus one and two are fairly common sexually transmitted viruses. Left untreated, neonatal herpes infections can cause devastating symptoms, including sepsis and severe neurological damage. Mothers and sometimes the newborns are treated with antivirals such as acyclovir. The management of neonates born with herpes simplex infections will be covered again in chapter seven.
- **Parvovirus B19**. This is a rather common virus that causes fifth disease, usually affecting children. Fifth disease is a completely benign illness in children and adults, giving mild fever and a rash. However, in fetuses, parvovirus B19 can cause a severe anemia that can result in a condition known as fetal hydrops. This can be fatal. This is one condition that can be treated by prenatal transfusion. However, only a few specialized centers perform the procedure.

- **Rubella**. This virus is usually covered by a vaccine, as was discussed in the prenatal care section. If the mother contracts rubella in the first and second trimester, it can lead to sensorineural deafness, eye abnormalities, and congenital heart defects.
- **Toxoplasmosis.** Toxoplasma is an intracellular parasite that mothers most often become exposed to through their cat. In a mother with a normal immune system, toxoplasmosis can be mild or even asymptomatic. However, for the fetus, toxoplasmosis can be fatal, especially if the mother is infected during the first trimester. Toxoplasma also causes a severe encephalitis that can cause permanent devastating brain damage.
- **Zika virus**. This virus is most common in Latin America, but it has been reported in the Southern United States. Zika is a mosquito borne virus. If a pregnant mother contracts Zika, there is an increased chance her fetus will develop microcephaly. The virus has been associated with other congenital central nervous system abnormalities as well.

Neonatology breakthrough: Decreasing vertical transmission of HIV

Earlier in the course, we discussed the most significant breakthrough in the history of neonatology, the 1959 discovery of pulmonary surfactant. However, it was twenty-one years later the first patient was treated with surfactant replacement therapy.

No other discovery has had an impact of this magnitude. However, the time interval between discovery and implementation has decreased somewhat. In 1994, the New England Journal of Medicine published the findings of the Pediatric AIDS Clinical Trials Group Protocol 076 Study Group. This was a trial designed to decrease vertical transmission of HIV. In this double-blind randomized trial, mothers were treated with the anti-viral agent azidothymidine. The mothers

were treated during the perinatal period and infants were then treated after birth. Treated mother and baby pairs were two-thirds less likely to contract the virus.

Even though the interval between the discovery of the human immunodeficiency virus and the pediatric AIDS trial was less than ten years, the story of the drug, azidothymidine, goes back further. The drug was developed in 1964 in an effort to create cancer chemotherapeutic drugs. However, zidovudine did not work and it was put on the shelf. Twenty-two years later it became one of the fastest-approved drugs in the history of the Food and Drug Administration. The clinical trial testing its activity against HIV was halted after only nineteen weeks because of its clear superiority in the treatment of HIV infections.

Key Takeaways

- The major objective of prenatal care is to reduce preterm birth and low birth weight.
- Prenatal screening looks for maternal infections, and other medical conditions that might impact the pregnancy, including anemia, high blood pressure, and pre-existing diabetes mellitus.
- The most important medical conditions managed in peri-natal medicine are gestational diabetes and pregnancy-induced hypertension.
- Most of the infections and drugs that do not directly cause congenital abnormalities can cause preterm delivery and/or low birth weight.
- Congenital anomalies may be malformations, dysplasias, or deformations.

Quiz

1. Which of the following is performed routinely during prenatal screening?
    a. Upper endoscopy
    b. Echocardiography
    c. Abdominal ultrasound
    d. Abdominal x-ray

Answer c. Abdominal ultrasounds are routinely performed to chart the growth of the fetus. Upper endoscopy is only done in cases of severe maternal gastroesophageal reflux. Echocardiography on the mother is not routine unless she has a previously undiagnosed heart murmur on physical exam. X-rays are contraindicated because of the small though measurable risk of fetal DNA damage.

2. What does the alpha fetoprotein test screen for?
    a. Neural tube defects
    b. Feeding tube defects
    c. Neural crest defects
    d. Neuromuscular defects

Answer a. The test is also a screen for chromosomal abnormalities such as Down syndrome.

3. What is the prenatal condition for which fetal blood transfusion is a therapy?
    a. Sickle cell anemia
    b. Megaloblastic anemia

c. Pernicious anemia

d. Parvovirus B19 related anemia

Answer d. Parvovirus B19 gives rise to a severe aplastic anemia that can lead to fetal hydrops. Fetal blood transfusion is curative.

4. Which anti-seizure medication is contraindicated in pregnancy?

    a. Valproate

    b. Benzoate

    c. Carbamazepine

    d. Valeric acid

Answer a. Also called, valproic acid is associated with neural tube defects such as spina bifida. Trade names include Depakote.

5. Which maternal autoimmune disease can affect the newborn?

    a. Multiple sclerosis

    b. Myasthenia gravis

    c. Rheumatic arthritis

    d. Grave's disease

Answer b. Maternal antibodies against proteins in the neuromuscular junction can cause transient hypotonia or respiratory distress in the newborn.

6. Which of the following is *not* associated with intrauterine growth restriction?

    a. Maternal diabetes mellitus

b. Maternal smoking

c. Low pre-pregnancy weight

d. Maternal trichomonas

Answer d. Many things cause intrauterine growth restriction, especially conditions that affect the placenta. However, mild vaginal infections such as trichomonas do not affect the fetus.

7. What is the incidence of twin births?

    a. one in seventy live births

    b. one in eighty live births

    c. one in ninety live births

    d. one in one hundred live births

Answer b. The rate is one in eighty births. The incidence increases with increasing maternal age and use of assistive technologies.

8. What is the definition of preterm delivery?

    a. Delivery at less than thirty-seven weeks gestation

    b. Delivery at less than thirty-eight weeks gestation

    c. Delivery at less than thirty-nine weeks gestation

    d. Delivery at less than forty weeks gestation

Answer a. Delivery at less than thirty-seven weeks gestation. Delivery between thirty-seven and thirty-eight weeks is considered late preterm. Thirty-nine or forty weeks gestation is considered full term.

9. Spina bifida is considered what kind of congenital abnormality?
    a. Disruption
    b. Deformation
    c. Dysplasia
    d. Malformation

Answer d. Though spina bifida can be caused by toxic insults or infections, it is nevertheless a developmental abnormality. Therefore, it is placed in the malformation category. Dysplasias describe abnormal development at the tissue level. Deformations are caused by problems in the uterus such as amniotic webs. Disruptions describe tissue breakdown that occur as after infectious or toxic insults.

10. Which of the following congenital infections is preventable by vaccination?
    a. Tetanus
    b. Rubella
    c. Cytomegalovirus
    d. Toxoplasmosis

Answer b. Measles mumps rubella vaccination is given to mothers who have low titers on prenatal screening. There is a tetanus vaccine, but tetanus is not a communicable disease. Cytomegalovirus and Toxoplasmosis do not have vaccines.

Chapter three: Delivery

In this chapter we will discuss the delivery process and various issues related to normal and abnormal deliveries.

First, we will discuss adaptation to life outside the uterus. We will then talk about some issues related to obstetric anesthesia that might affect the fetus. Then we will mention some of the steps involved in neonatal resuscitation and post-resuscitation care. Finally, we will cover issues related to intrapartum catastrophes such as hypoxic-ischemic encephalopathy and birth trauma. We will close with some points related to transfer of the newborn to a specialized care facility.

Adaptation to life outside of the uterus is a complicated process, involving several processes that happen almost simultaneously. The new physiological task of the newborn is to begin breathing air, after breathing only amniotic fluid for several weeks.

The process of birth shocks the baby's system. This is what causes the central nervous system response that stimulates the baby to take its first breath. There is a rush of catecholamines, commonly associated with the fight or flight response. A number of new stimuli may cause initiate catecholamine rush. The process of passing through the birth canal may provokes these changes. Likewise, the sudden change in temperature from warm to relatively cold may also have an effect.

Finally, there is the physical trauma of being handled outside the uterus. It is likely these processes collectively cause the catecholamine rush. It should be noted that this phenomenon occurs for babies born by cesarean section as well. Therefore, passage through the birth canal is

not necessary for stimulation of the first breath. Nevertheless, there is one disadvantage to cesarean section, and that is that there is not as much squeezing of fluid out of the lungs. We will return to this point shortly.

The first breath usually occurs within 10 seconds after delivery. If it is delayed, the attendant usually takes the newborn through a stage of resuscitation that we will cover shortly. It is recommended that the umbilical cord be cut within a few minutes of birth. The cutting of the cord, in combination with the catecholamine rush and the first breath leads to a number of physiological changes (Figure Seven).

- The arrival of room air oxygen in the baby's lungs causes decreased resistance in the pulmonary circulation.
- By Ohm's law, decreased resistance means that pulmonary blood flow suddenly increases. Prior to birth, most fetal cardiac output bypassed the lungs through the ductus arteriosus and the foramen ovale.
- The increase in pulmonary blood flow results in left atrial pressure being slightly higher than right atrial pressure, and this causes the foramen ovale to close. This new flow pattern causes a decrease in blood flow across the ductus arteriosus, the other fetal circulation bypass track.
- The increased oxygen content from breathing room air further causes the ductus arteriosus to constrict and close.
- What little amniotic fluid may have been left in the baby's is absorbed by the lung tissue.

- The catecholamine surge also causes a rapid acceleration in the production of lung surfactant, that began at about twenty weeks gestation.

The use of obstetric anesthesia can sometimes pass to the infant and causes what is called neonatal respiratory depression. The most common causes of neonatal respiratory depression are opioids and sedatives, especially when they are given systemically to the mother in the peri-partum period. If the mother requires general anesthesia, meaning intubation and inhaled anesthetics, these too can pass to the fetus and newborn. However, these effects are transient, and fade in minutes upon delivery, when the newborn's circulation separates from that of the mother. In recent years, the use of epidural anesthesia and regional anesthesia has improved newborn safety. In general, if an anesthetic is given in proper doses for an appropriately short period of time, there are no adverse effects on the newborn.

To help those attending the birth determine if any resuscitation efforts should be initiated, birth attendants rely on a system called the Apgar score. The Apgar score was developed by Virginia Apgar (Figure Eight), an anesthesiologist in New York City in 1952. The Apgar score grades five signs apparent in the newborn. Each sign is given a score of either zero, one, or two. The five signs are:

- Color: zero for blue or pale all over; one for blue at extremities only; and two for pink body
- Pulse: zero for absent; one for less than 100 beats per minute; and two for greater than 100 beats per minute.

- Irritability: zero for no response to stimulation; one for grimace on suction or aggressive stimulation; and two for cry on stimulation.
- Activity: zero for no activity; one for some flexion; and two for flexed arms and legs that resist extension
- Respiration: zero for absent; one for weak, irregular, or gasping; and two for strong, robust cry

Apgar scores are measured at one minute and again at five minutes. There is also a ten-minute Apgar score, but this is generally not measured unless the infant had very low initial scores and required resuscitation. The maximum score is ten, with two points in every domain. An interesting superstition has developed among maternity nurses regarding the score of a perfect ten. It is generally believed in maternal medicine that it is bad luck to give an infant an Apgar score of ten. Nurses will habitually subtract one point for color. Therefore, a healthy, robust newborn baby will most often be given a one-minute Apgar score of nine, and a five-minute Apgar score of nine. “Apgar scores nine and nine” is currently a shorthand way of communicating that the baby is perfectly healthy.

Lower Apgar scores are typically signals that resuscitation should be begun on a baby. Usually the birth attendants do not wait until one minute to begin efforts. If the baby does not take a breath within thirty seconds, or if the heart rate is below sixty beats per minute, efforts will be taken immediately to resuscitate the baby, as will be discussed shortly.

Low scores at one minute do not necessarily predict poor outcomes, especially if the baby pinks up and the heart rate recovers quickly between one and five minutes. However, persistently low

Apgar scores, at three or lower by ten minutes, suggests neurological damage that may be permanent.

Experienced midwives and maternity nurses are expert at recognizing a newborn that requires resuscitation. In an instant, there are three questions that can be asked and answered:

- Is this a term infant?
- Is the baby crying or breathing?
- Does the baby have good tone?

If the answer to all three questions is yes, the baby does not require resuscitation. These babies should not be separated from the mother, but should be dried quickly, the mouth suctioned quickly, and the body wrapped for warmth.

However, if the answer to any of the three questions is ‘no’, the nurse or midwife will do the following, in sequence during the first minute:

- Initial steps of resuscitation (provide warmth, clear airway if necessary, dry, stimulate)
- Bag-mask ventilation
- Chest compressions
- Administration of epinephrine and/or volume expansion, usually administered through the umbilical vein

If drying, warming, and clearing the airway does not stimulate respiration and heart rate, then bag-mask resuscitation is begun. Simply placing the bag over the baby’s nose and mouth, making a seal may be adequate. The small amount of positive pressure that is generated may be

enough to stimulate the baby to breathe spontaneously. If not, then positive breaths may be given with a bag. If the heart rate remains below sixty beats per minute, chest compressions are begun immediately. Preparations are made to intubate the baby. Generally, if the baby is born in a hospital, all of the necessary equipment is present at the bedside. Babies requiring this degree of resuscitation will be discussed in more detail below.

Once the baby's heart rate and respirations increase, the skin becomes pink and tone becomes more normal, the baby may be wrapped and brought to the mother.

Post-resuscitation care

Post-resuscitation care falls into two categories: care for the normal newborn, and care for the newborn who required more intensive resuscitation. For the normal newborn, with a high five-minute Apgar score, the baby will be observed closely, but can generally stay with the mother. Particular attention will be paid to the way that the baby feeds, and vital signs will be taken frequently. A baby who has one good breastfeeding of fifteen to twenty minutes is generally in good shape.

Breathing is also important to pay attention to. In particular, caregivers look for what is called grunting, flaring, and retractions. Grunting refers to a small sigh that a baby makes at the end of every expiration. This is an involuntary response on the part of the baby to raise end-expiratory pressure, thereby increasing oxygenation. Grunting is the earliest sign of respiratory distress and

is generally taken seriously. Grunting babies are taken either to the newborn triage area or to the special care area for monitoring and/or supplemental oxygen.

Flaring refers to nasal flaring. This is also an involuntary reaction on the part of the baby, who flares the nostrils open on inspiration in attempt to inhale more oxygenated air. It is unusual to have a baby who flares but who is not grunting. Retracting refers to inward movement of the skin between the baby's ribs on inhalation. This is a sign of increased respiratory effort, also a sign of respiratory distress.

The most common reason for grunting, flaring, and retracting occurring after a normal birth is an entity called transient tachypnea of the newborn. Transient tachypnea of the newborn is generally caused by retained lung fluid that does not clear during the process of birth. This is more common after cesarean deliveries than vaginal deliveries because in cesarean deliveries, there is less squeezing of fetal lung fluid. It generally appears within the first several hours of life. Likewise, transient tachypnea of the newborn lasts only for about six hours. It is sometimes referred to as transitioning, as it represents transition from the uterus to the outside world and is not a pathological condition. On chest x-ray, newborns with transient tachypnea of the newborn have diffuse streaky opacities in the lung fields, particularly in the fissures between the lung lobes (Figure Nine). The treatment involves at most supplemental oxygen in the form of an oxygen hood.

For the newborn that required more intensive resuscitation, the situation is somewhat different. Once the baby is stabilized, meaning the baby is breathing, with or without assistance, and has a

stable heart rate, the baby should be moved to a neonatal intensive care unit, or NICU. Many hospitals, even in smaller communities, have special care units where some interventions can be made to help the baby. Otherwise the baby is transported to a hospital with a high level NICU. We will discuss newborn transport shortly.

If a baby has respiratory depression, the reason may be exposure to opioids, as we discussed recently. Therefore, part of the resuscitation of the depressed newborn involves administration of the opioid-reversal agent naloxone. In addition, boluses of glucose-containing fluids are given, since hypoglycemia in the stressed newborn has been associated with negative neurological outcomes.

The special case in neonatal resuscitation is the case of hypoxic-ischemic encephalopathy, also called birth asphyxia. There are several possible causes of birth asphyxia, but they all share a common pathophysiology.

The fetuses' system is wired to favor oxygenation and circulatory nutrition to the brain. However, in situations where there is generalized hypoxia, particularly for long periods of time, the brain suffers hypoxic injury as well. Similarly, any other cause of reduced blood flow to the brain can cause birth asphyxia. Usually, birth asphyxia results from a combination of reduced hypoxia and reduced cerebral blood flow.

For the standard diagnosis of birth asphyxia to be made, all of the following features should be present:

- Severe metabolic or mixed acidosis, with umbilical pH less than seven from an umbilical artery.
- An Apgar score of zero to three for longer than five minutes.
- Seizures or hypotonia.
- Multiple organ involvement. These are usually diagnosed over the next few days after birth.

The signs of birth asphyxia typically occur within the first twenty-four hours of life. The baby's muscle tone may be greater than normal and the deep tendon reflexes may be more brisk than normal. In mild birth asphyxia, there will often be transient behavioral abnormalities, including poor feeding and irritability, expressed as excessive crying.

Moderate birth asphyxia is usually characterized by lethargy and hypotonia. The definition of lethargy is very specific in medicine. It does not mean simply a tired baby. Lethargy, to the pediatrician, refers to a neurological disturbance such that the infant sleeps until vigorously stimulated, and then returns to sleep when the stimulation stops. Hypotonia, as it sounds, refers to low muscle tone. It also refers to decreased deep tendon reflexes. Typical infantile reflexes, including the grasp and Moro reflexes, may be absent.

In more severe birth asphyxia, the infant may have periods of apnea. These are defined as cessation of respiration for twenty seconds or more. Apnea is usually accompanied by slowing of the heart rate, or bradycardia, as well. Seizures typically develop within the first twenty-four hours. They may be severe and may be resistant to conventional therapy.

Short of catastrophes like birth asphyxia, there are lesser forms of birth trauma that are important to know about. Simply put, birth trauma refers to injury that results from mechanical forces during delivery. Factors responsible for birth trauma may happen at the same time as birth asphyxia. In fact, the same factors that cause the injury may also cause asphyxia.

Birth trauma is common. It occurs about six to eight times per one thousand live births. It is the cause of two percent of all neonatal deaths and stillbirths in the United States. Nevertheless, most birth traumas are mild and resolve with expectant management or no therapy. About one half of birth injuries are avoidable if recognized in advance.

The risk factors for birth trauma include:

- Large-for-dates babies, especially those who weigh more than four and a half kilos
- Cephalopelvic disproportion means the baby's head is too big for the pelvic outlet, or the pelvic outlet is too small for the baby's head. Some abnormalities of the mother's pelvis can also cause cephalopelvic disproportion.
- Deliveries requiring instruments, especially high forceps and vacuum deliveries.
- Abnormal fetal lie, particularly breech presentation.
- Excessive or abnormal traction applied to the baby's body during delivery.
- Labor that is either too long or delivery that is too rapid.
- Very low birth weight or extremely premature infants, that are typically fragile.

The most common birth traumas are the following:

- **Soft tissue injuries**. These are usually bruises on the head from the vacuum (caput succedaneum, Figure Ten). There are also cuts and abrasions from instruments used in delivery.
- **Brachial plexus injury**. These are traction injuries, typically caused by excessive lateral extension of the baby's neck during delivery. The most common type of injury, called Erb's palsy, is characterized by weakness in the arm on the affected side. Up to ninety-five percent of Erb's palsy completely resolve during the first year (Figure Eleven).
- **Cranial nerve injuries**. These are also traction injuries, though they are more unusual than brachial plexus injuries. They are usually diagnosed on physical exam as facial asymmetries.
- **Laryngeal nerve injury**. Another unusual injury, laryngeal nerve injuries occur from abnormal head position in the uterus. The infant usually presents with stridor or a hoarse cry.
- **Bone injury**. Broken clavicle, or collar bone, is the most common fracture that occurs as a result of birth injury. Collar bone fracture is common in births of large-for-dates babies, especially ones in which the shoulder becomes stuck, called shoulder dystocia (Figure Twelve).

When a newborn requires a higher level of care than can be provided by the birth hospital or birth center, the infant requires transport. Typically, this transport will be to a hospital that has a NICU. If the NICU is not in the same hospital as where the baby was born, a transport team must go and retrieve the baby.

Most American NICUs have transport teams associated with them. The transport team may be a group of nurses and drivers that only transport, or they may be NICU staff that take turns, rotate into transport duties. The team members should be able to recognize impending respiratory failure in a newborn. There should also be at least one member who can perform effective bag-and-mask ventilation. This person, or another individual, should be proficient at intubation of newborns, especially premature infants. Neonatal veins are very difficult to access. The transport team may be the only individuals able to achieve venous access. This includes the umbilical vein, if it is accessible when the team arrives.

There are two special medications that are always carried by infant transport teams. One is artificial surfactant, and the other is prostaglandin. Surfactant is administered by endotracheal tube to substitute for the natural surfactant that a newborn may lack. Prostaglandin is a drug that keeps the ductus arteriosus open. This may be necessary to resuscitate some newborns born with complex cyanotic heart disease. In these infants, closure of the ductus arteriosus could result in shock or death. Finally, the team should be experienced in the management of neonatal ventilators. Typically, transported babies require bag-mask ventilation during transport. This usually occurs in a specialize transport incubator, important for temperature control.

Key takeaways

- The goal of delivery for the fetus is to convert from fetal circulation to mature circulation. This involves decreasing resistance in the pulmonary circulation
- Neonatal respiratory depression is usually due to opioid exposure. Naloxone is used for resuscitation.

- The Apgar score is used to assess the need for resuscitation and to predict neurological outcome.
- Hypoxic-ischemic encephalopathy, or birth asphyxia, results from generalized hypoxia, decreased cerebral perfusion, or both.
- Birth trauma is most often caused by cephalopelvic disproportion, often associated with large-for-dates babies.

Quiz

1. What is true about the ductus arteriosus?
    a. Prostaglandins cause the ductus arteriosus to close
    b. After birth, the ductus arteriosus must stay open if the foramen ovale closes
    c. After the birth, the ductus arteriosus must close.
    d. After birth, the increased pulmonary resistance causes the ductus arteriosus to close.

Answer c. Prostaglandins keep the ductus open, as may be necessary in certain types of congenital heart disease. The ductus and the foramen ovale generally close together. The resistance in the pulmonary circulation generally falls after birth.

2. Transient tachypnea of the newborn is:
    a. caused by retained fetal lung fluid.
    b. caused by failure of the resistance in the pulmonary circulation to fall.
    c. caused by a failure of the fetal lungs to produce surfactant.

d. caused by a paradoxical excess of lung surfactant.

Answer a. Failure of pulmonary resistance drop is called persistent fetal circulation. This will be discussed in chapter seven. Failure of the lungs to produce surfactant in full-term infants is a genetic condition. This too will be discussed in chapter seven.

3. Which of the following is not a component of the Apgar score?
    a. Color
    b. Bowel sounds
    c. Heart rate
    d. Irritability

Answer b. The other two of the five categories are breathing. and extremity tone.

4. Which of the following is *not* one of the questions you must ask regarding whether an infant requires resuscitation?
    a. Is this a high-risk delivery?
    b. Is this a full-term infant?
    c. Does the baby have good tone?
    d. Is the baby crying or breathing?

Answer a. High-risk infants may not necessarily require resuscitation at birth.

5. Which of the following are required in the delivery suite?
    a. IV fluid
    b. Infant bag-mask ventilator
    c. Incubator

d. Feeding tube

Answer b. The other items may be important, but not during delivery.

6. Which of the following is *not* an element of post-resuscitation care?
    a. Attention to hydration status
    b. Urine output
    c. Stool output
    d. Feeding

Answer c. Although important, monitoring for passage of the first stool is not an element of post-resuscitation care. It will become important later, as we will see in subsequent sections.

7. What is the most important cause of birth trauma?
    a. Extreme prematurity
    b. Precipitous delivery
    c. Fetal skeletal abnormalities
    d. Cephalopelvic disproportion

Answer d. The others are minor causes of birth trauma

8. What is the bone most often broken during delivery?
    a. The clavicle
    b. The femur
    c. The humerus
    d. Any of the cranial bones

Answer a. The other bones may be broken, but the clavicle is the most commonly broken.

9. Which of the following is a drug that infant transport teams typically carry with them?
    a. Ampicillin
    b. Prostaglandin
    c. Cortisone
    d. Amiodarone

Answer b. This is for keeping the ductus arteriosus patent in cases of certain types of congenital heart disease.

10. Which of the following is a reversal agent?
    a. Prostaglandin
    b. Midazolam
    c. Naloxone
    d. Hydrocodone

Answer c. Midazolam is a benzodiazepine, a sedative. Hydrocodone is an opioid, exposure to which may require naloxone therapy.

Chapter four: The normal newborn infant

In this chapter will discuss routine care, and the routine examination of the newborn. In addition, we'll cover topics related to support for the parents as well as feeding of the newborn. There will

also be a discussion of common problems that may arise during the first few days of life. Finally, we will discuss issues related to infants born to substance-using mothers.

Routine care of the infant begins at the moment of birth. From this moment on, the emphasis is on the formation of a bond between mother and baby. Current guidelines recommend that a baby not requiring resuscitation be left with the mother. Skin to skin contact is ideal, particularly as the infant would be experiencing something like cold-shock upon exposure to air. For this reason, newborns are frequently wrapped in blankets, usually two layers. In addition, the baby's head is covered with a hat. A disproportionate amount of body heat is lost through the head.

In the birthing suite, virtually all babies are given an intramuscular shot of vitamin K. This is because most babies are born deficient in vitamin K, and breast milk has very low levels of this vitamin. This shot is given because vitamin K deficiency can result in a rare but devastating newborn condition called hemorrhagic disease of the newborn. Vitamin K is a crucial component of the clotting system. Infants with hemorrhagic disease of the newborn can develop life-threatening intracranial hemorrhage. Even though this is an exceedingly rare condition, the risk-benefit rational of giving the shot is such that it is highly recommended.

In addition, most hospitals will place erythromycin ointment in the eyes of the newborn. This is done to prevent gonococcal ophthalmia. Prior to the practice of using erythromycin ointment, gonococcus was the most common cause of congenital blindness. Today the condition is rare. It is worth mentioning that gonococcal infection is screened for as part of routine prenatal screening. If a mother has gonorrhea, she is treated with antibiotics prior to giving birth.

It is unknown if erythromycin ointment prevents gonococcal ophthalmia in infants of mothers who tested negative for gonorrhea on prenatal screening. Some experts recommend withholding the ointment in gonococcus-negative mothers. This is because ointment interferes with the baby's ability to see their mother. Nevertheless, the practice of using the ointment is virtually universal in American maternity wards.

Standard recommendations state that newborns should be swaddled. Swaddling is defined as wrapping the newborn such that all major joints are maintained in flexion. This tends to be of the position the baby in the uterus. There are some variations. Some experts recommend swaddling with baby's elbows extended (such that the arms are held against the baby's sides). The hips and knees, however, are virtually always swaddled in flexion (Figure Thirteen).

Despite these recommendations, some newborns to take a strong dislike to swaddling. Many fight to free their arms. This is particularly the case for newborns who strongly desire to suck their hands, so some experts recommend allowing the infant to keep their arms free when swaddled. In general, swaddling is the best way to keep the infant warm, calm, and relaxed.

There is a great deal of controversy surrounding the use of pacifiers. Some advocates of breastfeeding argue that non-nutritive sucking interferes with breastfeeding. The scientific evidence for this is debated. Others suggest the pacifier should be offered at all times when the infant is not nursing. This appears to be the guideline adopted in most well-baby nurseries.

Some babies require sucking to remain relaxed more than do other babies. For these babies, the pacifier can be very good for the baby and caregivers, particularly mothers. Other babies reject the pacifier and never adapt to it. Most babies fall somewhere between the two extremes. Some babies, particularly premies and smaller normal newborns, may have difficulty keeping the pacifier in their mouths, or may inadvertently expel it with their tongue.

If a mother plans to breastfeed, she should receive support from caregivers and staff at hospitals. As paradoxical as it sounds, breastfeeding is a skill that a baby and a mother must learn. Whereas sucking is instinctive for babies, sucking from a human nipple is not.

For the mother, breastfeeding is definitely not instinctive, and must be taught. During the millennia prior to the advent of maternity hospitals, breastfeeding was taught by experienced mothers who had already breastfed infants. Despite the advances in medical care and technology, breastfeeding is still taught by experienced mothers. Today, those mothers tend to be maternity nurses as well as friends and family. For mothers who have difficulty despite help from others, many hospitals offer lactation consultations from licensed specialists.

A healthy full-term newborn only needs one good nursing session during the first twenty-four hours of life. The first twenty-four hours are a period of transition for the newborn which allows for recovery from the trauma of the birth process. Whereas a normal newborn will sleep twenty hours per day, a normal newborn may sleep more than this on the first day. Thereafter, the baby may nurse up to every two hours, or a total of twelve times per day. The normal range is eight to twelve times.

Current guidelines recommend that the infant spend as much time with the mother as possible. Nevertheless, virtually all maternity wards include a nursery where babies may be attended by maternity nurses. This is particularly helpful for tired and stressed mothers. Even for babies that room in with their mothers exclusively, nurses are required to perform various duties for the babies.

During the first day of the baby's life, the nurse generally bathes the baby, unless the mother objects. This is often an opportunity for the new parents to learn how to bathe the baby. In addition, the nurse will weigh the baby daily. It is expected that a normal full-term baby will lose up to ten percent of their birth weight during the first two to three days of life. This is normal. Nevertheless, the ten-percent weight loss figure is considered by some hospitals to be a threshold at which a breastfed baby should be given formula supplementation. The scientific evidence to support this practice is contested.

In addition, nurses take baby's vital signs, generally heart rate and respirations. They also record urine and stool output. Unless directed to make quantitative measurements, urine and stool output is generally noted qualitatively. It is especially important that a baby make urine and stool during the first day of life. Failure to urinate might indicate that there is a problem with the genitourinary system or that the baby is severely dehydrated. Failure to pass the first stool, called meconium, may be a sign of a problem with the neuromuscular structure of the rectum. In addition, while measuring heart rate and respiratory rate, the nurse will note the presence of murmurs or abnormal breath sounds. These are reported to the medical staff if found.

Newborn nurseries also routinely measure blood pressures. The normal range of blood pressure is different for a newborn than for even an older infant. The same is true of respirations and heart rates. The maternity nurses generally only alert medical staff if any of these parameters are grossly abnormal on their exam.

In addition, some maternity wards are measuring blood pressure in all four extremities. This is done especially in cases where they hear a murmur. This is a screen for certain rare congenital abnormalities of the circulatory system, such as coarctation of the aorta. Nurses also perform measurement of hemoglobin oxygen saturation with a device called a pulse oximeter. Now with current guideline to screen for congenital heart abnormalities, the oxygen saturation is also measured in more than one extremity.

A hearing screen is also performed, generally during the second day. This test is called a brainstem auditory evoked response test, or "BAER" [pronounced "bear"] (Figure Fourteen). With the newborn quietly sleeping in a quiet room, small headphones are placed and two electroencephalogram leads are placed on the baby's scalp. The baby's brain response to tones at various frequencies are measured. If the recordings fail to record responses to the tones, the baby is referred for more intensive testing by a hearing specialist. Hearing screens have been very helpful in detecting cases of congenital deafness. This has allowed early intervention for the babies to acquire communication skills at a very early age.

Inborn errors of metabolism are also screened for on the second day of life. Most states have newborn screening programs that vary slightly from one another. These programs are designed to screen for several extremely rare inborn errors of metabolism, and one very common one, congenital hypothyroidism. Congenital hypothyroidism was the most common cause of mental retardation in the United States. However, hypothyroidism is easily treated with daily thyroid replacement therapy. Today, thanks to newborn screening programs, mental retardation due to hypothyroidism, also called cretinism, has become vanishingly rare. The medical expenditures saved by preventing cretinism more than compensate for the cost of screening for the other, rarer inborn errors of metabolism.

These blood tests are performed via a heel stick, generally after the first twenty-four hours of life. Metabolite levels change substantially during the first day of life. For this reason, newborn screening tests are calibrated to measure metabolite values for the second day of life. The blood is sent to a testing facility as dried drops of blood on filter paper. Test results often return within two days. If any test results are out of the normal range, the infant is referred for more comprehensive testing.

Most states test for thirty-two inborn errors of metabolism. Some states screen for many other conditions as well. Massachusetts screens for sixty-four metabolic errors. Although hypothyroidism is by far the most common and the most treatable, newborn screening is known as PKU. This is name of another test in the panel, that screens for the condition known as phenylketonuria.

The following is a list of the classes of common tests. It is by no means necessary to memorize this list. It is sufficient to remember hypothyroidism and phenylketonuria.

- **Amino acid metabolism defects.** These babies are unable to digest certain proteins. Phenylketonuria is one such defect.
- **Congenital infections.** In most tests, this means toxoplasmosis, discussed in the prenatal screening section.
- **Cystic fibrosis.** The most common recessive genetic disease among Caucasians.
- **Endocrine disorders.** This is the class where hypothyroidism is found
- **Enzyme deficiencies for vitamins and sugars.**
- **Fatty acid oxidation disorders.** These babies cannot metabolize fatty acids
- **Hemoglobinopathies.** These include sickle cell anemia and thalassemia.
- **Severe Combined Immunodeficiency**.
- **Urea cycle disorders.**

The purpose of any screening test is to help diagnose a disease before it becomes symptomatic, so that treatment can be initiated. The list of thirty-two tests on the newborn screening panel include some disorders that generally manifest before the test results are known. These disorders tend to be the ones in which the infant is congenitally unable to digest certain proteins. These infants become ill often by the second day of life, by the time the test is being drawn. For these babies, the heel-stick test is not a screening test as much as it is an aid in making a diagnosis for a disease process that has already begun.

Other tests screen for entities for which there is currently no effective treatment. The screen for hemoglobinopathies is a good example. In this sense, the screening tests help make a diagnosis, but do not guide treatment.

The baby's first vaccine can also be given in the hospital prior to discharge. This is the vaccine for hepatitis B. It will be the first of the total series of three vaccines. It is the only routinely given vaccine that can be given shortly after birth. For babies born of mothers with known hepatitis B disease, or in whom hepatitis B status is not known, the baby is also given a dose of immunoglobin specifically enriched for antibodies against hepatitis B virus. Studies suggest that this combination reduced maternal-newborn transmission of hepatitis B virus. There is no evidence that early vaccination in hepatitis B negative mothers prevents the disease in newborns.

In American maternity wards, it is standard practice that a pediatrician or family medicine doctor examine the newborn within the first twenty-four hours. In addition, the newborn is generally examined every day the baby is in the hospital. For a normal vaginal delivery, this generally means two exams, as the family is discharged after forty-eight hours. For cesarean deliveries, the mother is permitted to stay for four nights. Therefore, the baby is often examined by the doctor up to five times prior to discharge.

The newborn physical exam

The physical exam takes place either in the mother's room or in the nursery. Keep in mind that the physician has already read the chart and the nurse's notes. This way, the physician can pay particular attention to findings that have already been noted, though a comprehensive exam will

be performed. The lights must be turned up such that the physician is able to see the baby's skin color well. The baby is generally completely unclothed for the exam. If the baby has not yet been bathed, the examiner usually wears gloves.

The exam proceeds from head to toe. Nevertheless, there are portions of the exam that must be done with the baby quiet and not crying, so the exam sections may be performed out of order while the infant is quiet and relaxed. Of these, the most important is the eye exam. While the room is still darkened, the physician uses an ophthalmoscope to look into the baby's pupils. What she is looking for is the so-called red reflex. The retina should appear reddish pink in a normal newborn. If it appears white, this may be a sign of an extremely rare congenital tumors called retinoblastoma. If possible, the physician may also check to see if the pupils are reactive to light during this exam (Figure Fifteen).

In addition, while the infant is quiet, the physician may also listen to heart sounds and breath sounds. For breath sounds, it may be sufficient to check that they are present on both sides. The exam for heart murmurs is more challenging. The normal newborn heart rate is one hundred twenty to one hundred sixty beats per minute. Listening for murmurs requires a sensitive and experienced pair of ears. The stethoscope used has a head with a diameter of about two centimeters, small enough to hear heart sounds with interference from breath or bowel sounds.

The most common murmur encountered on the first day of life is the murmur of the patent ductus arteriosus. As we noted, this outlet usually closes shortly after birth. However, when the first exam occurs during the first four hours of life, the ductal murmur is often observed. It is best

heard at the left upper sternal border. It is usually gone by the second day of life. If the murmur has not gone by the second day, further testing occurs. This includes, among other things, a chest x-ray and four-extremity blood pressures.

Once the quiet parts of the exam are completed, a fuller head to toe exam may follow. The first part of the exam is the overall impression. Does the child's head, body and extremities appear symmetric and normally shaped? Is the fat and muscle tone appropriate for gestational age? The appearance of the skin is also important. The physician is particularly concerned with detecting jaundice. This is possible even in very dark-skinned babies by examining the gums. Neonatal jaundice is discussed later in this chapter.

The physician turns her attention to the skull, particularly the size and location of the two fontanelles, or openings between the bony plates of the skull. Contrary to popular belief, there are in fact two fontanelles (Figure Sixteen). These are the well-known anterior fontanelle, and the smaller, sometimes pinpoint posterior fontanelle. Both should be open. In addition, attention is paid to the plates themselves, to ensure that none are prematurely fused. This condition is called craniosynostosis. If found, a neurosurgeon is consulted. The physician also takes note of the position and shape of the ears. Low-set or posteriorly-rotated ears may be a sign of a previously undiagnosed syndrome, though the sign is non-specific.

The mouth begins with observing the gum line. Sometimes white inclusion cysts are noted. These are perfectly normal, but parents may be worried by them, and it is important to reassure them. The tongue exam is important only for looking for the presence of a tongue tie (Figure

Seventeen). This refers to a web of tissue from the floor of the mouth to the underside of the tongue. There is a great deal of controversy as to whether tongue-ties should be separated in the nursery. Some infants nurse perfectly well even with severe tongue ties. Others do not. Likewise, some children born with tongue ties develop perfectly understandable speech, while others do not. Macroglossia, or large tongue, can be a sign of various genetic disorders including Down syndrome and Beckwith-Wiedemann syndrome (Figure Eighteen). Finally, the physician should attempt to obtain a gag reflex. It is not necessary to severely gag the newborn, such that she vomits or has trouble breathing. Placing a gloved finger on the soft palate gently usually elicits the reflex.

The exam proceeds to the neck where the examiner is primarily interested in finding intact clavicles. Recall that broken clavicle is the most common form of birth trauma. A broken clavicle will feel crepitant below the examiner's fingers. If a broken clavicle is suspected, the physician may order an x-ray for confirmation (Figure Nineteen).

The shape of the chest is noted, particularly the shape and placement of nipples. Supernumerary nipples are rare, and they have no significance. Nevertheless, nervous parents may notice them. It is worthwhile to inform them so they are not surprised later. Often, small skin tags are noted. These may be ligated with suture thread and may fall off on their own. Larger skin tags may require a dermatology consult. Some infants have a prominent xiphoid [ZY-foid] process at the most inferior portion of the sternum (Figure Twenty). As with most of these findings, a prominent xiphoid is completely benign, but it may worry parents. If discovered, it should be pointed out and explained to parents.

The abdominal exam begins with observation, as to most parts of the physical exam. Many examiners first look at the umbilical stump. This is to ensure that there are three vessels: one vein and two arteries. Anomalies of the number of umbilical vessels may occur in various syndromes (Figure Twenty-one).

The shape and movement of the abdomen is observed. In other parts of the physical exam, auscultation, or listening, is performed last. However, in the abdominal exam, auscultation is done after observation. This is because percussion and palpation cause changes in bowel sounds that might interfere with the auscultation exam. The examiner is listening for tinkling bowel sounds. Absence of bowel sounds would be unusual but is a serious sign that would warrant an x-ray. High-pitched hyperactive sounds may be signs of an obstruction, commonly accompanied by a distended appearance.

Finally, the examiner palpates the abdomen. A liver edge is looked for but is not always found. The spleen is difficult to palpate in a normal newborn. Because the newborn has very thin abdominal musculature, it is easy to feel stool masses. This is very important to note, particularly in a newborn that has not yet passed a first stool. In this regard, it is important to verify that there is a patent anus. Congenital absence of the anus is rare but is extremely important to note after birth. This is so that a surgeon can be consulted.

The genital exam is usually next. It is important to note that the newborn had until recently been bathed in high concentrations of maternal progesterone. The infant's own endocrine system had

been particularly active toward the end of gestation. For these reasons, the skin on the genitalia may appear darker than in an older infant. In addition, they may be relatively larger than they will be in an older infant.

In female newborns, because of this hormone effect, there may be more whitish secretions than parents might expect. In addition, there may be hypertrophic vaginal tissue that extrudes from the vaginal introitus (Figure Twenty-two). This is a perfectly normal finding but may alarm parents. In addition, small amounts of blood may be apparent within the vagina. This can be extremely alarming to parents. There are some persistent cultural beliefs surrounding this phenomenon. In fact, vaginal blood or "witch's blood" is perfectly normal, being caused by the same hormonal changes already discussed. This should be explained to parents.

In male newborns, the examiner is looking for the presence of a chordee, or bent penile shaft, because of fibrous attachments (Figure Twenty-three). The examiner is also looking for the penile opening, to ensure that it is present at the tip. Hypospadias, or displacement of the urethral tip, is rare, but a fixable condition (Figure Twenty-four). If the parents were requesting circumcision in the hospital, either chordee or hypospadias need to be identified first. These findings may delay circumcision until the conditions are repaired.

It is also important in boys to verify the presence of two testicles. Undescended testis is a common finding. It often resolves on its own. However, if it does not, the testis is surgically brought down into the scrotum later in childhood. If one or both testes are not found in the scrotum, the examiner traces the path of the presumed spermatic cord back to the inguinal

region. The missing testis is sometimes found there. An exam for the presence of inguinal hernia is sometimes done at this time. The examiner uses the smallest finger to look for the presence of a space in the inguinal canal wide enough to accept the finger. If noted, a surgeon may be consulted.

The extremities are examined next. The examiner is primarily interested in symmetry and tone. Does the infant move all four extremities equally? If not, it may be a sign of some form of birth trauma such as broken clavicle or brachial plexus injury. Next, attention is paid to muscular tone. A full-term infant is fully flexed at the elbows, hips and knees. However, these joints should be easily extended without exerting too much force. The grasp reflex is elicited by placing the thumb in the palm of the newborn's hands. The newborn should reflexively grab the finger.

Next, the examiner elicits the Moro, or startle reflex (Figure Twenty-five). After eliciting the grasp reflex, the examiner gently pulls up on the newborn's arms. It is not necessary to lift the baby off the cushion. Then the examiner lets go. The baby should reflexively make a hugging motion, as if to grab something that is not there. Some believe the Moro reflex may have evolved because the infant needs to hold on to its mother. The ability to re-grasp the mother after losing grasp may confer selective advantage.

The wrists and the ankles are hyperflexible and hyperextensible at birth. The feet may be internally rotated, as they were in the uterus. The key point of this exam is to ensure that both wrists and ankles move in both directions. Congenital club foot may be diagnosed in this fashion.

The ankles are also tested for the presence of clonus, elicited by rapid flexion. One beat of ankle clonus is normal. More than one beat may indicate a spinal cord problem.

The last deep tendon reflex tested is the patellar tendon reflex. No equipment, such as a Taylor hammer, is required for this exam. The examiner gently taps the patellar tendon with the tip of a finger which should elicit a fairly brisk kick.

The last part of the extremity exam is designed to screen for congenital dislocation of the hip. The two tests the examiner performs are called the Barlow and the Ortolani maneuvers (Figure Twenty-six). The infant must be quiet and relaxed for this exam. If agitated, the babies increased muscle tone at the hips might interfere with the exam. The examiner holds one newborn leg in each hand, with the knee in the palm and the tip of the middle finger on the greater trochanter of the newborn's femurs.

For the Barlow maneuver, with the baby's hip and knee in flexion, and internally rotated, the examiner presses down into the cushion. No movement should be present. For the Ortolani maneuver, the examiner externally rotates each hip in sequence. If there is a congenital dislocation of the hip, this is the maneuver most likely to reveal it. The examiner will feel a noticeable "clunk" as the head of the femur displaces anteriorly. If there is a "click" instead of a clunk, this is unlikely to represent a dislocation, but should still be followed up. In any case, the exam is repeated every day the baby is in the hospital, and at well-baby exams.

Finally, the examiner picks up the newborn and performs a back examination. Of particular interest here is the presence of a sacral dimple. If these are deep and accompanied by tufts of hair, they may indicate neural tube defects. Because a sacral dimple may not be accompanied by any abnormalities, when finding is noted it may simply be followed up over time. In addition, the examiner notes if the gluteal skin folds are symmetric. Asymmetry may be another sign of a congenitally dislocated hip.

Not every part of the exam is repeated every day. For example, the red reflex need not be elicited at every exam. If it was present once, this means there is no retinoblastoma. Similarly, the gag reflex is unlikely to disappear spontaneously from one day to the next.

Parental support

Having discussed the routine physical and neurological exams of the newborn, we will now mention some points related to support of the parents. The first few days of life can be extremely stressful, even for experienced parents. It is important to recognize that the sleep deprivation associated with labor, delivery, and the first few days of life place stress on a mother and her family. This is the case regardless of the number of children she already has. Maternity nurses are expert at detecting mothers who could use their assistance. They may keep the baby in the well-baby nursery several hours at a time to allow the mother to sleep.

It is also possible to enlist the help of fathers, partners, or other caregivers. Anything that does not involve breastfeeding can be accomplished by someone other than the mother. Hospital staff should encourage participation by these caregivers for the mother's sake.

For new mothers and her partners, the stresses can be particularly acute. Oftentimes, the most valuable support that hospital staff can provide is reassurance. After all, the staff is the most experienced regarding babies, and they certainly know what is normal and what is not. If there are normal findings that a parent may not have noticed, it is best to point it out. The finding should be explained calmly and patiently. All parental questions should be answered.

Nevertheless, everything regarding baby care may be new to first-time parents. They will have numerous questions, and may ask them repeatedly (remember, they are sleep-deprived!) Because everything related to baby care is new, parents will be watching staff closely to learn what they do by example. It is important to explain the difference between the hospital and home. For example, new parents may not realize that it is not necessary to take the baby's temperature every eight hours.

Similarly, many experienced baby nurses will place babies on their sides in the newborn nursery. Sometimes the bassinet is angled up. This is done because the newborns are being observed at all times. Parents, noticing this, may put the baby down this way at home. However, the American Academy of Pediatrics recommends that newborns be placed supine on a flat surface. This is done to reduce the incidence of sudden infant death syndrome. These important differences should be explained to parents.

Feeding

Feeding, or difficulty feeding, is often the largest source of stress for parents. Here, a great deal of patience and persistence is required to help parents though the difficult first several days.

There is little doubt, on the basis of decades of study, that human breast milk is the best for newborns. However, support for breastfeeding requires a multi-pronged approach. The strategy should begin before birth. Mothers usually have an idea prior to delivery as to whether they want to breast feed. This is a screening question that is always asked when a woman is admitted to deliver a baby.

Mothers need to be told early and often that their breast milk does not come in at the moment of birth. This can require a full forty-eight hours. Because of this delay, and because of the rules regarding hospital discharge, a mother and her baby may be home before her milk comes in. It is important to explain to her the value of colostrum. She should know that this first milk is rich in antibodies and nutrients that will help protect and prepare the baby.

The process of learning to breastfeed can be extremely frustrating. It is easy for a new mother to become distraught and anxious at this point. Hospital staff need to acknowledge this frustration and offer particularly attentive support. Successful breastfeeding mothers usually accept advice from several different sources. What she needs to understand is that every piece of advice she hears will be different and will not all be true. This goes for advice that appears to be contradictory. What works for one mother will not work for another. The mother will find a system that works for her and her baby. In the meantime, she will need all the tips and tricks offered.

If the mother simply does not want to breastfeed, her decision should be supported. A baby who is formula feed should receive one to two ounces every four hours. This will roughly equal what would be received breastfeeding every two hours.

Formula-fed babies will be gassier than breastfed babies. This is because of the air in bottles. Formula-fed babies may poop less often than breastfed babies. A breastfed baby will poop roughly with every feeding. A formula-fed baby may poop half as often. The expected frequency should be explained to parents.

However, it is important that parent not become obsessive about counting poops. The same goes for nursing and wet diapers. Once a consistent feeding and elimination pattern develops, parents should stop obsessively charting these parameters. This piece of advice may be extremely reassuring to stressed parents.

Minor abnormalities of newborns

In this section, we will discuss some minor abnormalities that occur in the first few days of life. All of these are likely to occur in the hospital, so there is the opportunity to explain to parents that these findings will disappear, never to return.

Periodic breathing is one sign that can be particularly alarming. Periodic breathing is a fetal pattern of chest movement. The infant breathes deeply and audibly for four to six breaths, then takes four to six shallow breaths. The latter are so quiet that they cannot be heard, and it does not

appear that the infant is breathing. Explain to the parents that this is the breathing pattern the baby had in the uterus, and that it will pass after a few days. It is perfectly normal and does not harm the baby.

Meconium, or the first stool, can be disturbing to see, particularly if the parents are not prepared for it (Figure Twenty-seven). Meconium can be dark green to dark brown (never jet black). The consistency of meconium can be anything between rubber cement and three-day pan grease. In any case, meconium is extremely difficult to clean off skin. Parents need to be told that they need to apply a fair amount of force to clean off meconium. They need to be told they will not harm the infant if they do this. As meconium transitions to normal yellow baby stool, the color will pass through all shades of green. It will be easier to wipe the baby. By the time the parents become expert at cleaning meconium, it will have passed.

Urate crystals are reddish substances that are created by the newborn's kidneys in the first few days of life, during the period of relative dehydrated (Figure Twenty-eight). The parents may be alarmed when they see this in a diaper because it looks like blood. In truth, it looks more like facial rouge than blood. If staff members find urate crystals before parents, they should point this out so that the parents are not surprised.

In addition to these minor abnormalities, there are a number of common problems of full term infants that are important to review here.

Spitting up is an extremely common problem. By definition, spitting up is a form of gastroesophageal reflux. By definition, milk that starts in the stomach and ends up outside the babies body is reflux. However, there are lesser forms of reflux, in which milk does not quite reach the epiglottis, where it may or may not trigger a cough. It is important to stress that the term “acid reflux” has no meaning, especially for newborns. All reflux is acid reflux because the stomach is acidic. Not all infants suffer symptoms because of acidic stomach contents entering their esophagus and mouth.

The first question to ask is whether the infant is gaining weight. After the initial ten-plus percent weight loss, a healthy term infant will gain one to two ounces per day. If this is occurring, the quantity of reflux is likely not excessive. However, if the infant is not gaining weight, or appears to be distressed by the refluxing, action should be taken. Signs that the newborn is distressed would be arching, grimacing, and coughing. In this case, the first step would be to recommend that the infant’s body be angled up thirty degrees on a flat plane and kept on this angle at virtually all times except during diaper changes. This is often sufficient to solve the problem.

If angling the newborn’s body does not decrease symptoms, treatment with anti-acid medications may be used in addition to angling. A good first step would be to use a histamine two receptor blocker such as ranitidine. The most common brand name is Zantac. If after several days there is no effect, ranitidine may be replaced by a proton pump inhibitor such as omeprazole. Contrary to popular opinion, omeprazole can begin to work in a day or two. The classic teaching is that the full therapeutic effect requires one week for all the proton pumps to be covalently modified.

If these medical therapies fail, one may consider thickening feeds in addition to medical therapy and angling. Thickening feeds means adding a component to formula to allow gravity to discourage stomach liquid from refluxing. An alternative to all these interventions is smaller, more frequent feeds. This can sometimes decrease the quantity of reflux. However, some infants are enormously disturbed by interrupting feeds. The crying that results may end up worsening the situation.

Nasal congestion is a common problem of full term infants. It is related to reflux, because milk often ends up in the nasal cavity and the mouth. This phenomenon may give the mistaken perception that the infant has allergies. Nasal environmental allergies are rare in newborns. Newborns are obligate nose-breathers. This means that, unless they are crying, they are breathing through their noses. Therefore, managing nasal congestion is important. If the nasal congestion interferes with nursing or sleeping, intervention should occur. In addition to using the "angle technique", caregivers should not be afraid to use gentle suction in the nose. If local irritation is responsible, parents should be encouraged to keep a cool mist humidifier running by the bassinet or crib. This device should be cleaned daily to avoid mold formation.

Also related to reflux is the question of formula intolerance. There is a great deal of confusion in the community regarding the difference between formula intolerance and lactose intolerance. Lactose intolerance, or the relative inability to digest lactose, is virtually unheard of in newborns. Formula intolerance means the infant does not tolerate formula. This may be evident by excessive gas, fussiness, or spitting up frequently. A small number of these instances of formula intolerances are milk protein intolerances. If so, a formula switch should be recommended. If the

baby is nursing, the mother should perform an elimination diet. The latter involves cutting out one type of food at a time until the baby's intolerance resolves.

An even smaller number of these cases are true allergies. The most specific sign of true protein allergy is blood in the stool. The baby's anus should be examined for fissures to make sure there is no other source of blood.

Anal fissures are another common problem of full-term infants. These are small cuts in the anus that result from forceful pooping. The baby may become constipated through involuntarily stool retention to avoid the pain. Anal fissures are treated with over the counter antibiotic ointment. They heal very quickly.

Epstein's pearls are tiny white balls that appear on the roof of the mouth and occasionally the gum line (Figure Twenty-nine). These are inclusion cysts that occur during the fusing of structures during development. They are completely normal and resolve without treatment.

Baby acne appears during the first month of life (Figure Thirty). It is the result of withdrawal from mother's hormones as they clear from the baby's circulation. There is no specific treatment for baby acne and it resolves completely within days.

Peeling skin is particularly common for post-dates babies. These are babies born at forty-two weeks or later. It can also occur in newborns after birth as they approach forty-two weeks

gestational age. The peeling skin does not bother the baby. The treatment is generous use of a hypoallergenic moisturizer.

Substance using mother

Questions regarding alcohol, tobacco and drug use are usually asked when a mother is admitted to deliver her baby. It is not unusual for mothers who use substances to honestly report the used substances during pregnancy. However, they may not always be honest about the last time they used a substance. Nevertheless, if they admit to substance use, the baby's meconium will be collected and sent for drug testing. If the meconium is positive, it suggests that the baby was exposed to the substance in utero. Some states also perform tests on baby's hair or urine.

If the baby's meconium is positive, it does not necessarily mean that the baby will be removed from the mother. This depends heavily on the state and their various laws.

In only three states, substance abuse during pregnancy is a crime. These are Alabama, South Carolina, and Tennessee. Nevertheless, women have been prosecuted for drug use during pregnancy in all but five states. In eighteen states, laws are on the books stating that drug use during pregnancy constitutes child abuse. In only three states (Wisconsin, Minnesota, and South Dakota), detection of drugs in a woman prenatally is considered grounds for civil commitment of the mother.

However, none of these laws indicate the likelihood that the newborn will be eventually reunited with the mother, regardless of the outcome of treatment. These outcomes are complex results of interactions between state laws and judicial discretion.

However, a social worker will be assigned to interview the mother regardless of the outcome of the test. This is done to offer help to the mother and her baby. The best outcome for all would be a healthy newborn going home with healthy parents.

Infants of opioid mothers are a special case. Opioid withdrawal in infants can give distressing symptoms. These include irritability, feeding problems, excessive crying, and gastrointestinal problems. These babies are often treated with low-doses of a mild opioid. The dose is weaned very slowly. These babies must stay in the hospital during their treatment.

Fetal alcohol syndrome deserves special mention here. For much of our history, fermented beverages were the drinks of choice, as potable water was scarce. The process of making beer and spirits removed microorganisms, although the manufacturers could not have known this.

From the 1960s to the 1980s, alcohol was used as a tocolytic, to halt preterm labor. Ethyl alcohol was even administered intravenously. The side effects were actually worse than you might expect, and the practice was discontinued.

The earliest causal connection between alcohol and adverse birth outcomes was made in 1899. Incarcerated British women who were alcohol abusers had far higher rates of stillbirths than non-

drinking cell mates. The recognition of the full-spectrum of fetal alcohol syndrome did not emerge until its description in the literature in 1973.

A diagnosis of the fetal alcohol syndrome may be established when the following four criteria are met:

- Proven or suspected use of alcohol during pregnancy.
- Growth deficiency: height and/or weight below the tenth percentile.
- Characteristic facial features: these are smooth philtrum, thin vermilion portion of the lips, and small palpebral fissures (Figure Thirty-one).
- Central nervous system damage: This must include structural, neurological, or functional damage

One of the most important factors to keep in mind regarding the fetal alcohol syndrome is that the spectrum of expression is extremely broad. There may or may not be a dose-relationship with alcohol and the manifestations of fetal alcohol syndrome. However, it appears that the syndrome is more common as a result of pregnancies where the mother drank heavily during the first trimester. In the later trimesters when much of development has already been completed, the characteristic dysmorphic features are unlikely to be present.

Key takeaways

- A number of screening tests are performed after birth for several congenital abnormalities and infections.

- The physical exam of the newborn is designed to screen for several developmental abnormalities.
- Support for parents after birth focuses mostly on feeding, particularly breastfeeding.
- Minor normal abnormalities parents may encounter in the first few days include meconium, urate crystals, and periodic breathing.
- Gastroesophageal reflux, or spitting up, is the most common problem of term infants.

Quiz

1. What is the most important inborn error of metabolism that is captured on newborn screening?
    a. Sickle cell anemia
    b. Phenylketonuria
    c. Hypothyroidism
    d. Galactosemia

Answer c. The money saved by avoiding cretinism pays for the cost of the test for all the other inborn errors of metabolism

2. What is the purpose of a screening test?
    a. To treat a disease before it appears.
    b. To diagnose a disease before it appears.
    c. To diagnose and treat a disease before it appears.
    d. To cure a disease before it appears.

Answer b. The point of a screening test is to identify a disease before it becomes symptomatic. The test itself is not a treatment or a cure. In this sense, many of the tests for inborn errors of metabolism are not true screening tests. This is because several of the diseases appear before the test result comes back. In other cases, knowing the diagnosis does not alter the course of the illness.

3. What congenital infection is tested for on newborn screening?
    a. Cytomegalovirus
    b. Rubella
    c. Herpes simplex I and II
    d. Toxoplasmosis

Answer d.

4. What do Barlow and Ortolani's maneuvers test for?
    a. Congenital dislocation of the hip
    b. Congenital clavicle fracture
    c. Congenital retinoblastoma
    d. Congenital hypotonia

Answer a. Clavicles are examined by palpation. Retinoblastoma is diagnosed with the ophthalmoscope. Hypotonia is observed globally.

5. How often does a normal full-term newborn breastfeed?
    a. every hour

b. every two hours

c. every three hours

d. every four hours

Answer b.

6. How much formula does a normal full-term infant take at each feed?

    a. half to one ounce

    b. one to two ounces

    c. two to three ounces

    d. three to four ounces

Answer b.

7. Which of the following is a minor abnormality in the first few days of life?

    a. Hip clunk

    b. Baby acne

    c. Urate crystals

    d. Red reflex

Answer c. Hip clunk is a physical exam sign of congenital dislocation of the hip. Baby acne occurs at around two weeks of life. The red reflex is a physical exam finding.

8. What is the cause of baby acne?

    a. Hormonal withdrawal

    b. Erythromycin ointment

c. Formula protein intolerance

d. Congenital adrenal hyperplasia

Answer a. As the condition occurs as a result of withdrawal form maternal sex hormones that are being cleared from the newborn's system.

9. What is the most common cause of a newborn heart murmur?

    a. Patent foramen ovale

    b. Patent ductus arteriosus

    c. Patent pulmonary artery

    d. Patent coronary artery

Answer b. This murmur disappears as the ductus closes, from four to twenty-four hours after birth.

10. Which of the following is *not* a screening test done in the nursery?

    a. Hearing screen

    b. Vision screen

    c. Newborn screen

    d. Cardiac anomaly screen

Answer b.

Chapter five: the sick newborn

In this chapter we will discuss the sick newborn. We will specifically talk about admission to the neonatal intensive care unit and the developmental peculiarities of premature infants that impacts care in the NICU. We will also discuss the stabilization of the sick newborn. Finally, the sick newborn chapter will discuss the most important issue relating to NICU care, namely respiratory support.

Except in rare circumstances, the only patients admitted to a NICU are newborns within hours of birth. Rarely are babies admitted to NICUs who have previously been discharged home. Newborns who have gone home and quickly become ill are admitted to regular pediatric wards. The reasons for this mostly have to do with infection control. Once a newborn has gone home, they are more likely to contract pathogens not present in the hospital. NICUs are extremely concerned with infection control, as are other parts of the hospital. However, premature infants are particularly susceptible to infections. Therefore, NICUs place tight restrictions regarding admission.

Of course, a newborn may be admitted to a NICU who has been born outside of the hospital. For example, newborns delivered precipitously at home (or on the way to the hospital) may suffer birth traumas such as those discussed in the previous chapter. However, the overwhelming majority are transferred from a maternity ward or birthing center. In general, there are six reasons why a newborn infant would be admitted to the NICU:

- **Prematurity** - for reasons that will be discussed in more detail in chapter six.

- **Respiratory distress syndrome** - or relative pulmonary surfactant deficiency. This can occur in full-term infants, but is primarily a condition of premature infants.
- **Sepsis** – these are systemic infections. NICUs are particularly adept at managing sepsis in newborns.
- **Hypoglycemia** – NICUs manage low blood glucose levels more often, and with a higher degree of expertise than do standard pediatric wards.
- **Perinatal depression** – perinatal depression often results from a hypoxic-ischemic insult. It can also result from exposure to perinatal anesthesia and other causes.
- **Maternal chorioamnionitis** – This is an ascending infection of the amniotic fluid and membranes. It usually occurs after rupture of membranes. The newborn is not necessarily affected by the infection. Nevertheless, NICU admission may be indicated at the discretion of the hospital staff, for reasons that will be discussed in subsequent sections.

Neonatal intensive care units are locked wards. There is always a unit secretary on post who screens everybody seeking admission to the NICU. Often, meetings with families and/or consulting services take place outside the NICU. If visitors are ill, or suspect they may be ill, they are denied entrance. Strict control of who enters the NICU is for infection control and patient safety.

If one is permitted entrance, the guest immediately encounters a scrub room where all visitors, including physicians, must thoroughly scrub their hands before entry. Shoes must be covered with booties. In addition, individuals must where gowns and masks. Gloves are always worn if

the patients are to be handled, though they need not be sterile gloves. The latter is reserved for sterile procedures.

The specific developmental needs of premature infants explain what the visitor will see upon entrance to a NICU. NICUs are not like other areas of the hospital. The lighting is always relatively dim. There are no brightly flashing lights. The windows do not permit outside light. The reason for the subtle light is because the stimulation may interfere with overall nervous system rest that premies require. The only places where the light may be more intense are warming tables, where the very smallest premies may be found. The staff caring for these babies must be able to see everything clearly. The premies are given eye covering to protect them from more intense light.

The room is much quieter than other sections of the hospital. Music never plays. There are no overhead speaker systems. Instead, there are intercom systems that call only the particular bedside where a patient or NICU staff member may be found. Even the alarm bells on incubators (also known as isolettes) and intravenous pumps are quieter and subtler than in other parts of the hospital.

The quiet nature of the NICU is specifically designed to reduce stimulation. Loud and sudden noises trigger startle reflexes in premature infants. Infants who are being tube or bottle fed experience feeding interruption and reflux in response to loud noise. Noise may even trigger apnea and bradycardi events.

Tactile stimulation can likely disrupt the therapeutic program in the NICU. Though the newborns must be examined and fed. Nevertheless, contact with the premies is kept to a minimum. There are some exceptions.

Kangaroo care is the practice of permitting skin-to-skin contact between the newborn and a parent (Figure Thirty-two). The concept of kangaroo care originated in Colombia. A shortage of incubators led to the use of parents as human incubators, even twenty-four hours per day. Studies in Colombia showed substantial declines in premature infant mortality. The practice of kangaroo care then spread throughout the world. Currently, kangaroo care is practiced for one to three hours per day, not twenty-four hours as in the original Colombian studies. Even the smallest infants undergoing mechanical ventilation can do kangaroo care.

Full-term newborns who are born ill, or who become ill shortly after birth, are also admitted to neonatal intensive care units. The same rules regarding sensory stimulation apply to full-term newborns. Though NICUs are generally divided into two parts, as we will discuss shortly, these larger newborns are not segregated from the premies. Rather, they are permitted to benefit from the same reduced sensory stimulation conditions as the premies.

The division in the NICU has to do with the intensity of the level of care. The highest level, for the sickest and smallest patients, generally is where the infants receiving mechanical ventilation are cared for. The other section is for newborns that require a lesser intense care. Typically, premature infants who wean off respiratory support move to this section. In general, these infants

are already feeding by mouth and can regulate their temperature without an incubator. They are sometimes referred to as “feeders and growers”.

The stabilization of the sick newborn involves aspects of both newborn resuscitation and infant transport. Very often, it will be NICU staff that stabilize a sick newborn either in the delivery room or in the course of a transport procedure. An infant should be stabilized to the greatest extent possible prior to being placed in an ambulance or helicopter for transport.

The principles of newborn stabilization are the same as for any sick patient. They begin with the ABCs: airway, breathing, and circulation. The assessment of respiration begins with observation. As discussed in a previous chapter, grunting, flaring, and retracting are signs of respiratory distress. Tachypnea in a newborn is defined as breathing rate more than sixty breaths per minute. The infant is also observed for the presence of cyanosis. If grunting, flaring, retracting, tachypnea, or cyanosis is noted, respiratory support is begun. This begins with verifying that the airway is clear. Subsequently, the stabilization team will provide oxygen, continuous positive pressure, nasal cannula, or bag-mask ventilation.

Premature infants will be intubated where they are encountered, usually in the birth suite. Recall that transport teams carry artificial surfactant with them. After the airway is secured and an endotracheal tube is in place, a chest x-ray will be taken to confirm placement. After proper placement is verified, a dose of surfactant will be given causing an increase in chest compliance within minutes. This is because the open alveolar units will more easily ventilate in the presence of surfactant.

After airway and breathing are established, attention is paid to circulation. Heart rate and pulses are measured. Recall that a newborn with a heart rate below sixty beats per minute will receive chest compressions, even as the airway and breathing are being stabilized. Blood pressure is taken, but a more accurate measurement of perfusion is capillary refill. The newborn's fingers or toes are squeezed briefly. Then the number of seconds is counted until the digit becomes pink again. A capillary refill time less than two seconds is normal. Any period longer than this suggests that the infant may be in shock.

In a newborn, shock is the state of inadequate oxygen supply to tissues to meet demands. The following are possible reasons for shock in a newborn. All of these possible causes should be addressed, or at least considered, when stabilizing a sick newborn.

- **Hypoxic-ischemic event** – These are often because of peripartum catastrophes such as were discussed in the previous chapter. Metabolic acidosis is the main reason for circulatory collapse and poor cardiac output.
- **Sepsis** – The final common endpoint of the effects of overwhelming infection is peripheral vasodilation. This is accounts for the drop in cardiac output associated with septic shock.
- **Inborn errors of metabolism** – We discussed these in general in a previous chapter. The inborn errors responsible for metabolic acidosis can give rise to shock.
- **Hypovolemia** – The most common causes are blood loss as in a perinatal catastrophe such as placental abruption.

- **Congenital heart disease** – This is particularly true for anomalies that require a patent ductus arteriosus to perfuse the brain and vital organs. As the ductus closes after birth, the infant may experience circulatory shock. This is why infant stabilization teams carry prostaglandin.
- **Mechanical obstruction** – Anything that impedes return of blood flow to the heart will cause a rapid decline in cardiac output and shock. Mechanisms include tension pneumothorax, congenital diaphragmatic hernia, and pneumopericardium.
- **Arrhythmia** – Although rare, neonatal arrhythmias may prevent the heart from delivering adequate cardiac output.

The key to stabilizing a sick infant is rapid identification of these conditions and attempts to reverse them as quickly as possible. Rapid volume replacement, with a bolus of normal saline, is a standard first step to attempt to reverse acidosis and hypovolemia. We will discuss congenital diaphragmatic hernia in more detail in chapter seven. For now, it is enough to recognize that a nasogastric tube placed to suction may relieve the mechanical obstruction that can relieve circulatory shock. Pneumothorax and pneumopericardium are treated with needle aspiration of air. Cultures are taken and broad-spectrum antibiotics are given empirically, to treat presumed sepsis. These will be continued until culture results are known. If necessary, pressor agents are given to boost the newborn's blood pressure, and hence cardiac output.

Once circulation is stabilized as much as possible, the infant may be treated for the underlying disease. If the infant requires transport to a NICU, the transport team can now safely move the infant.

Once the infant is stabilized, there are a number of options available to support respiratory status. The mildest is blow-by oxygen. An oxygen source is held near the baby's face. This may be enough to decrease the baby's respiratory muscle demand. If blow-by is not adequate to maintain a good oxygen saturation, a nasal cannula with higher-flow oxygen may be placed. If this is inadequate, continuous positive airway pressure may be applied. This may involve the use of a mask that delivers oxygenated air at a pressure of about five centimeters of water. The increased positive end-expiratory pressure provided may be enough to help the newborn oxygenate their blood.

Ventilatory assistance

More intensive respiratory support includes positive pressure ventilation, or what is commonly referred to as a respirator. Intubation and mechanical ventilation of premature and other infants has some important differences with these procedures in adults. Cuffed endotracheal tubes are not used for infants, this is because the narrowness of the trachea is such that a cuff is not necessary to prevent dislodging. To the contrary, cuffed tubes would be more likely to traumatized the trachea than to secure the endotracheal tube.

There is only one purpose of ventilation assistance. This is to support the newborn's breathing until she can breathe on her own. Assisted ventilation may be needed to help the newborn through a transient period of newborn depression. It may also be needed for longer periods, as when a premature infant has immature lungs and respiratory centers.

There are three types of mechanical ventilation in newborns including: positive airway pressure, conventional mechanical ventilation, and high frequency ventilation.

Continuous positive airway pressure

Continuous positive airway pressure may be thought of as the least invasive of the assisted ventilatory efforts. Via a tight-fitting mask or an endotracheal tube, a stream of oxygenated air is applied to maintain a constant pressure, usually at around five centimeters of water in pressure. The benefit of this approach is that it increases the volume of alveoli that might otherwise collapse. A direct result of alveoli being more inflated is that accumulated lung water redistributes to the vascular space. The match between ventilation and perfusion of airways thereby improves. However, overly high levels of positive airway pressure may be harmful.

The underlying principle of this type of ventilation is that it overcomes one of the biggest physiological problems of newborn lungs. That is, decreased functional residual capacity. Functional residual capacity may be thought of as the bottle of air out of which an individual breathes. In adults, the bottle is relatively large. This explains why if we voluntarily stop breathing, even without taking a large breath, our blood oxygen saturation will not immediately decrease. This is because we have a reserve of oxygenated air in our airways. In infants, this so-called bottle of air is very small or is non-existent. As a result, very small increases in resistance or work of breathing will compromise the system and the infant will desaturate. Continuous positive pressure overcomes this problem by artificially creating a larger bottle of air for the newborn to breathe.

Conventional mechanical ventilation

Continuous positive airway pressure may be superior to positive pressure ventilation because it minimizes pressure trauma to the lung. Nevertheless, mechanical ventilation may be necessary. The best way to figure out what kind of assistance the newborn needs is to understand the basic pathophysiology of her particular respiratory disorder. The goal is to provide good gas exchange without overly traumatizing the lungs.

Adjusting the settings on mechanical ventilators can seem as much like an art as a science. Finding the appropriate peak inspiratory pressure to provide is most often done by visual inspection. The operator observes the newborn's chest and tries to set a peak pressure that causes the chest to rise as much as it would during a normal breath. In newborns with non-compliant chests, as is often the case in respiratory distress syndrome, higher peak inspiratory pressures may be necessary. The downside of higher pressure is more barotrauma and higher risk of bronchopulmonary dysplasia. The diagnosis of this entity will be discussed in more detail in a future chapter.

The next important parameter to consider in mechanical ventilation is the end-expiratory pressure. The reason to maintain at least some end-expiratory pressure is to keep alveolar units from collapsing, and to keep adequate functional residual capacity. However, too much end expiratory pressure can be a bad thing. If the pressure at the end of expiration is too high, venous return may be inhibited. Cardiac output would then drop as would oxygen transport.

The last important parameter to consider is the rate of ventilation. Most neonatologists favor a strategy of high rate, low tidal volume. A delicate balancing act is performed to maximize oxygen delivery to the tissues while minimizing mechanical damage to the lung tissue.

High frequency ventilation

High frequency ventilation is used exclusively in newborns. An entirely different principle underlies this modality. Gas transport occurs via convection, rather than injection of puffs of oxygenated air. The true reasons why high frequency ventilation works are not completely understood. However, they may involve improved gas exchange between lung units, increased turbulent flow, and improved gas diffusion. Adequate tidal volume may be delivered despite very short inspiratory times.

High-frequency jet ventilation delivers gases from a high-pressure source via a narrow cannula. The fast flow of oxygenated air creates areas of relative negative pressure that pulls in gases from their surroundings. High-frequency flow interruption delivers small tidal volumes as well. But it does so by interrupting the flow of the pressure source. One of the most commonly used high frequency modalities is oscillatory ventilation. In this method, very small volumes are delivered, even smaller than the dead space at extremely high frequencies.

Other modes of ventilatory assistance

Other respiratory interventions include inhaled nitric oxide. This has been shown to be effective for newborns with persistent pulmonary hypertension. Finally, the most intensive respiratory intervention is extracorporeal membrane oxygenation. This is essentially a heart-lung machine. It

is used only when it is expected that the disease process in the newborn is likely to last only for a few days. Once the respiratory and circulatory systems have recovered, the heart-lung machine may be weaned down and discontinued.

Key takeaways

- NICUs are meant to be low-sensory stimulation, clean environments.
- NICUs have two levels. The higher level is designed for mechanical ventilation. The lower level is for feeders and growers.
- The principles of newborn stabilization are based on the ABC-principle: airway, breathing, and circulation.
- Stabilization and transport teams carry surfactant and prostaglandin to begin management of some of the causes of instability in newborns.
- Definitive treatment may begin once the infant is stabilized.

Quiz

1. What is not required to be worn in a NICU?
    a. Sterile gloves
    b. Mask
    c. Gowns
    d. Booties

Answer a. Gloves should be worn when handling patients, but they need not be sterile

2. NICUs provide sensory protection for all the systems except:
    a. Visual
    b. Auditory
    c. Taste
    d. Touch

Answer c. The other systems are all calmed through low light, low noise, and limited touching.

3. What is the basis of kangaroo care?
    a. Reduced tactile stimulation
    b. Skin-to-skin contact
    c. Reduced exposure to light
    d. Reduced noise stimulation

Answer b.

4. What are patients in lower-level NICUs called?
    a. Full-term infants
    b. Late-preterm infants
    c. Stabilized infants
    d. Feeders and growers

Answer d.

5. All of the following are signs of respiratory distress except:
    a. Poor capillary refill

b. Grunting

c. Flaring

d. Retracting

Answer a. This is a sign of circulatory failure.

6. Tachypnea in a newborn is defined as respirations greater than:

    a. Thirty breaths per minute.

    b. Forty breaths per minute.

    c. Fifty breaths per minute.

    d. Sixty breaths per minute.

Answer d. Newborns have much higher respiratory rates than older infants and children.

7. Which of the following is a source of mechanical obstruction that can give rise to newborn shock?

    a. Ductal-dependent cardiac malformations

    b. Congenital diaphragmatic hernia

    c. Sepsis

    d. Placental abruption

Answer b. Ductal-dependent lesions are a cause of drops in cardiac output. Sepsis causes circulatory collapse. Placental abruption is a potential source of hypovolemic shock. Congenital diaphragmatic hernias are space-occupying lesions in the chest that can mechanically impede return of blood flow to the heart.

8. What medication does the stabilization team use to improve lung function?
    a. Prostaglandin
    b. Surfactant
    c. Ampicillin/Gentamicin
    d. Dopamine

Answer b. Prostaglandin is used to preserve cardiac output in some infants with complex congenital heart disease. Ampicillin/Gentamicin are antibiotics given to treat presumed sepsis. Dopamine is a pressor.

9. What kind of respiratory support reduces pressure trauma?
    a. Blow-by oxygen
    b. Nasal cannula oxygen
    c. Positive pressure ventilation
    d. High-frequency oscillatory ventilation

Answer d.

10. What conditions are appropriate for treatment with extracorporeal membrane oxygenation?
    a. Sepsis
    b. Complex congenital heart malformation
    c. Hypoxic-ischemic encephalopathy
    d. Congenital rubella syndrome

Answer a. Appropriately-treated sepsis can be reversed in a handful of days. The other conditions are permanent. Extracorporeal membrane oxygenation is only appropriate in situations where the disease process is likely to reverse quickly.

Chapter six: the preterm infant

In this chapter we will discuss medical problems that are unique to the premature infant. We will cover general issues including growth and nutrition and temperature regulation. However, the bulk of the chapter will be occupied with discussing problems by organ system. Finally, there will be a short section on anticipated outcomes in premature infants.

It is an oversimplification to attribute all conditions with premature infants to their immaturity. Similarly, claiming the premature baby is not prepared for life outside of the womb is not specific enough. The best way to explain the unique problems of premature infants is to discuss the three vital actions required to survive outside of the womb: Premies must breathe on their own, eat on their own, and must regulate their own body temperature. Until the newborn can do these three things, hospital care is required.

Temperature regulation

As discussed, vitals signs for a normal newborn are very different than normal vital signs of older infants and children. However, there is one vital sign that is the same for all humans: body temperature. Many premature infants struggle to maintain a normal body temperature while wearing normal infant clothing. This may have to do with a premies relative absence of

subcutaneous fat. However, this is overly simplistic. Humans have evolved to remain in the uterus for approximately forty weeks. The metabolic systems needed to maintain a normal body temperature do not develop until about thirty-five weeks gestation. Until that time, premature infants require warming units. These may be either warming tables or isolettes.

There are four ways an infant loses body heat: radiation, convection, conduction, and evaporation. Radiation refers to the electromagnetic energy that all bodies emit or absorb in proportion to temperature differences. Newborns may lose heat from a cold wall near their bed or may gain it from a heat lamp on a warming table. Conductive heat losses occur through direct contact. This may be a cold receiving blanket or cold air. Pre-warming blankets and even intravenous fluid can reduce conductive heat loss.

Convective heat loss occurs via moving air or water. Heat leaves a newborn's body when the air near their skin is colder than their own temperature. Convective heat loss is even greater in the delivery room. Here the infant is transferred into a relatively cold room. In the process of being moved to a warming table, the newborn rapidly loses heat by convection through the cold air.

Evaporative heat loss occurs through skin or the respiratory tract when water turns to gas. The rate of this evaporation depends on the vapor pressure gradient between the newborn and the outside world.

Studies indicate there are several ways to prevent heat loss in the delivery room. These include increasing the temperature and using heated humidified gases. In addition, using exothermic or thermal mattresses as well as heat loss barriers may help.

Many maternity units deliberately elevate the temperature specifically to reduce neonatal hypothermia. In addition, they provide humidified gases instead of dry gas. Thermal mattresses and plastic wraps have also been used, with remarkable success.

The baby's temperature is monitored constantly with a skin monitor. When the newborn graduates to feeder and grower status, temperature is measured only every four hours with a standard thermometer. During the process of transition from the isolette to an open crib, the temperature of the heating unit is gradually decreased to room temperature. When the infant is maintaining normal temperature, movement to an open crib is allowed.

Babies are unable to maintain their body temperature until about thirty-five weeks; Similarly, they are not ready to feed on their own until about thirty-five weeks. From an evolutionary standpoint, this makes sense. The fetus is fed via the umbilical cord until birth. By the time of birth, the newborn's gastrointestinal system is ready to digest proteins and simple carbohydrates. The rate of growth is fairly rapid during the last trimester of pregnancy. The fetus will be gaining one ounce per day. This is more or less thirty grams per day.

However, eating involves more than chemical digestion. The newborn must be able to suck and swallow in a coordinated, sequential fashion. This seemingly simple sequence is actually an

extremely complex series of reflexes and muscular movements. The fetus generally does not develop a coordinated suck and swallow until thirty-five weeks gestation. Females tend to develop this capacity quicker than males.

Necrotizing enterocolitis

There is an important gastrointestinal problem of premature infants that is worth mention. This is necrotizing enterocolitis. The pathophysiology of necrotizing enterocolitis is unclear. However, it is fairly certain that it has something to do with the immaturity of the gut. The disease is characterized by a brisk inflammatory response within the walls of the small intestine and colon. It is frequently accompanied by systemic infection.

The peak time of onset is typically second to third week of life in premature infants. It also tends to occur more often in formula-fed infants. The pathology involves various types of injury to the intestinal tract, ranging from mucosal injury to necrosis and even perforation.

Necrotizing enterocolitis occurs in almost ten percent of premature infants weighing less than one and a half kilograms. Depending on its severity, as many as half of infants with the condition will die from it.

Symptoms of necrotizing enterocolitis include the following:

- Feeding intolerance
- Increased abdominal girth and distension
- Visible intestinal loops through the abdominal wall

- Decreased bowel sounds
- Changes in stool pattern
- Hematochezia, or bloody stool
- Palpable abdominal mass
- Redness of the abdominal wall

The pathognomonic sign on x-ray is “train-track” lucencies in the wall of the intestine (Figure thirty-three). This is a radiographic sign of air in the bowel wall. The presence of free air seen on x-ray is an ominous sign of perforation. In such cases, emergent surgery is indicated. Similarly, the appearance of gas in the portal system is a marker of poor outcome. In addition, the following laboratory findings may aid the diagnosis:

- Moderate to severe neutropenia strongly suggesting sepsis
- Anemia from blood loss due to hematochezia and/or a developing consumptive coagulopathy. However, accumulation of extravascular fluid may result in paradoxical hemoconcentration.
- Thrombocytopenia

The treatment of necrotizing enterocolitis depends on its severity. However, the mainstays of treatment are as follows: cessation of enteral feeds, nasogastric decompression, and antibiotics. It is unclear whether the condition can be prevented. However, there has been some positive results from studies of breast milk-fed premature infants.

The lung

As with the gut, the fetal lung generally becomes fully mature by thirty-five weeks of life. At this point, the cells of the alveoli are creating their own surfactant. Surfactant is the substance that allows spherical alveoli to remain open throughout the respiratory cycle. In the absence of surfactant, the alveolar air units collapse. Without surfactant, it requires a substantially larger amount of energy to open a collapsed alveolus.

In cases of preterm labor, the stress imposed on the mother and her fetus cause secretion of endogenous corticosteroids. These cause the fetus to rapidly create surfactant. To aid this process, mothers in preterm labor are often treated with the steroid betamethasone. This helps accelerate the fetus's own surfactant production. Nevertheless, this small amount of surfactant production is often inadequate.

Respiratory distress syndrome

One of the most common respiratory conditions of prematurity is respiratory distress syndrome. The name is somewhat misleading. The signs in the newborn are certainly indicative of respiratory distress. There is tachypnea, grunting, flaring, and retracting. But at its basis, respiratory distress syndrome is the deficiency of pulmonary surfactant. Insufficient numbers of airways are ventilated, and relatively deoxygenated blood returns to the heart. Hypoxia is the result.

The diagnosis is made by history and x-ray (Figure Thirty-four). On x-ray, the lung volumes are lower than expected. Recall that too few airspaces are open because of low surfactant levels. In addition, the lung fields have the appearance of ground glass. This is also described as diffuse

airspace and interstitial opacities. The diffuse nature of the airspace disease helps differentiate respiratory distress syndrome from neonatal pneumonia.

Premature infants requiring respiratory support are treated with artificial surfactant. This is delivered via endotracheal tube. Sometimes, several doses are given over a period of days. As a result of surfactant treatment, the x-ray appearance improves rapidly and dramatically. After the initial period of respiratory distress and surfactant treatment, the infant may still require mechanical ventilation until they are able to make enough of their own surfactant. In addition, the infant needs to recruit an adequate number of lung units to adequately oxygenate blood.

The process of assisting a premature baby's respiration has its costs as well. The lung tissue is damaged by prolonged use of oxygen and positive pressure. If the baby requires supplemental oxygen to remain well-saturated for at least twenty-eight days, by definition, the baby has bronchopulmonary dysplasia. Like respiratory distress syndrome, bronchopulmonary dysplasia is a misleading name. The baby's lungs are not dysplastic or did not develop abnormally. To the contrary, they developed normally. Their further development and maturation were interrupted by therapy in the NICU. The nature of the damage is inflammation caused by oxygen and positive pressure. Therefore, it would be more correct to call this bronchopulmonary disruption, according to our definition of birth defects in chapter two.

Biographical sketch: Mary Ellen Avery

By the mid-twentieth century, neonatology was no longer the province of obstetricians and anesthesiologists. By this time, trained pediatricians were taking care of the smallest newborns.

Therefore, it is not surprising the next great breakthrough in neonatology was discovered by a pediatrician, Mary Ellen Avery (Figure Thirty-five).

Dr. Avery was born in New Jersey in 1927. The Avery's next-door neighbor was a female pediatrician who triggered Mary Ellen's interest in pediatrics. Dr. Avery attended Johns Hopkins Medical College, one of only four women in her class. After graduation, she contracted tuberculosis, igniting Dr. Avery's interest in lung diseases. After recovering and returning to pediatrics, Dr. Avery came to Boston, where she made her revolutionary discovery.

While observing the differences between infants who died of respiratory distress syndrome and full-term infants who died of other causes Dr. Avery discovered pulmonary surfactant. She published her findings in 1959. However, it took twenty-one more years before Dr. Avery's findings were translated into clinical practice. In 1980, the first successful trial of surfactant replacement therapy was published. Dr. Avery lived to see the fruits of her labor. Between the 1960s and Avery's death in 2011, deaths from respiratory distress syndrome declined by over ninety percent.

Bronchopulmonary dysplasia

The full criteria for bronchopulmonary dysplasia are these four features:

- Baby needs positive pressure ventilation for at least the first two weeks
- Baby needs supplemental oxygen for longer than twenty-eight days
- Respiratory distress develops when respiratory assistance is weaned or withdrawn

- Chest x-ray showing diffuse hyperinflation with cystic changes

There is currently no effective treatment for bronchopulmonary dysplasia. Steroid treatment can have an effect in some cases. The best strategy is to avoid development of bronchopulmonary distress in the first place. This is done by limiting exposure to oxygen and positive pressure to the greatest extent possible.

Even if the premature infant passes through the critical stage of surfactant deficiency unscathed, there is still yet another problem. Breathing is not an automatic process. It is controlled by the respiratory center of the brain. This cluster of neurons do not fully mature until around thirty-five weeks of life. It is said that a premature infant "forgets to breathe." This is only a figure of speech, but in the sense the brain is not doing its job, it is correct.

Apnea

The clinical consequence of forgetting to breathe is what is called apnea. Literally, this means without breath. By definition, apnea is failure to make a respiratory effort for twenty seconds. When apnea occurs in a premature infant, it is called apnea of prematurity. These apneic events are usually accompanied by a slowing of the heart rate. Therefore, in NICUs, the events are usually referred to collectively as apnea and bradycardia. Sometimes, the shorthand expression "spell" is used.

The spells of the apnea of prematurity can be classified into three groups:

- **Mild spells** are very brief and resolve spontaneously before a nurse has a chance to try and stimulate the baby. They generally occur once or twice per day.
- **Moderate spells** involve both apnea and bradycardia. They may include oxygen desaturation. These spells require a nurse to jostle the baby gently to stimulate breathing.
- **Severe spells** are characterized by long periods of apnea and substantial bradycardia. They are associated with oxygen. These require substantial stimulation. Sometimes they require blow-by oxygen or positive pressure ventilation.

As the baby matures, the spells become less frequent. Some special care nurseries require that a baby be spell-free for a certain number of days before going home. This is to ensure that no further apnea and bradycardia events occur at home. For more severe cases, caffeine is given as a central nervous system stimulant.

The premature brain

The lungs and intestines are not the only organs that can suffer damage. There is also the premature infant brain. Prematurely born babies are particularly sensitive to brain injury. The most common site of injury is the lining of cells surrounding the third ventricles of the brain, called the germinal matrix. The resulting injury is called intraventricular hemorrhage. There are four grades of intraventricular hemorrhage, depending on the severity of the bleed. The prognosis of the injury depends on grade of the hemorrhage. Grade three and four hemorrhage are most closely associated with cognitive and physical deficits.

Periventricular leukomalacia is a more severe form of brain injury in premature infants. It is estimated that three to four percent of premature infants weighing less than one and a half kilos develop periventricular leukomalacia. Approximately four to ten percent of infants born before thirty-three weeks gestation have the condition. Periventricular leukomalacia is characterized by necrosis, and later scarring, of the white matter surrounding the third ventricle.

There is a spectrum of consequences of periventricular leukomalacia. These include developmental delay, cerebral palsy, and seizures. There is no specific treatment. As with intraventricular hemorrhage and bronchopulmonary dysplasia, the best approach is to avoid prematurity.

It is also important to mention the effects of prematurity on the premature infant's eyes. The retinopathy of prematurity is not directly a consequence of prematurity. Rather, it results from supplemental oxygen treatment.

Retinopathy of prematurity is characterized by disorganized blood vessels in the retina. This may result in scar formation and retinal detachment. As with the brain damage just discussed, there is a spectrum of damage. Retinopathy of prematurity may be mild and may resolve spontaneously. When more severe, it may lead to blindness. The treatment is laser ablation of the peripheral retina. This can be performed in the NICU.

Moving down to the heart. On several previous occasions we have mentioned the patent ductus arteriosus (Figure Thirty-six). We will now discuss why a patent ductus is a problem and how it

is managed in the NICU. A patent ductus arteriosus permits some oxygenated blood from the aorta to flow backwards into the pulmonary artery. From there it goes to the lungs. The flow moves in this direction because the pressure is higher in the aorta than in the pulmonary artery. If too much blood flows in this direction, the newborn may become short of breath. All the extra blood flowing to the lungs makes the work of breathing harder for the baby. This extra work requires an enormous number of calories. But the infant cannot keep up with the caloric demands because it is too difficult to feed because of the increased work of breathing. This vicious cycle is what is called congestive heart failure.

There are two treatments for patent ductus arteriosus, one medical and one surgical. The medical treatment is indomethacin, a non-steroidal anti-inflammatory related to ibuprofen. Indomethacin has the opposite effect as prostaglandin. Recall that prostaglandin is used to keep a ductus arteriosus patent. Indomethacin is used to close the ductus. The other treatment is surgical ligation. This is done either via thoracoscope or internally via coiling.

Infections

We will now discuss infections that can occur in preterm infants in the NICU. The spectrum of infections that occur are different from what are seen in general pediatrics. In two large single-center studies, the most common bacterial infections in NICUs were caused by Staphylococcus and Klebsiella. Blood stream infections, urinary tract infections, and pneumonia were most common. The reason for the predominance of staph infections may have to do with the large number of invasive catheters that are used. Outbreaks of infections with similar organisms are taken very seriously in NICUs. When NICUs become colonized with pathogens such as

pseudomonas, the hospital often closes the unit and the patients are transferred to other units or hospitals.

In our discussion of necrotizing enterocolitis, we mentioned that the condition is treated in part with antibiotics. This is because of invasion of the gut mucosa by bacteria that are already present. In this sense, the condition is an infection, although it was not communicated to the infant by a caregiver or a visitor.

Jaundice

The treatment of jaundice in the NICU deserves considerable attention. We will discuss jaundice in some detail in chapter seven. However, in premature infants, elevated levels of bilirubin are particularly dangerous. This is because the blood brain barrier is weaker than in full-term infants. Many premature infants are also sick, with sepsis or other shock syndromes. These hyper-inflammatory situations predispose the premature infant to the toxic effects of bilirubin.

Neonatal intensive care units have a very low threshold to treat elevated bilirubin levels. It should be mentioned that very high percentages of premature infants receive therapy for jaundice. The therapy is virtually always light therapy. It turns out that bilirubin is converted to a form that can be eliminated in the urine. This form is created by photoisomerization of the bilirubin that is formed when the infant's red blood cells are destroyed. It was discovered that intense blue light is best to generate the photoisomerization reaction.

Recall from our earlier discussion that intense light is discouraged in the NICU. To manage the use of phototherapy the infant's eyes are shielded during therapy. The baby is kept in an isolette or warmer, undressed except for the diaper, so as to maximize skin surface exposed to the blue light.

Anemia of prematurity

Regardless of gestational age, all newborns have a drop in hemoglobin levels after birth. This is usually of no consequence for term infants. However, for premature infants, the anemia can be pathological. The anemia may also be exaggerated by the numerous blood tests that a premature infant invariably undergoes. This secondary anemia has been referred to sardonically as "the anemia of chronic investigation". Nevertheless, oxygenation is absolutely essential for tissue growth and repair. Therefore, anemia should be treated aggressively, with transfusion if necessary.

The condition known as osteopenia of prematurity is very commonly encountered in the NICU. Osteopenia, or relatively low mineralization of bone, has many causes. There is an inadequate supply of vitamin D, calcium, and phosphorus. In addition, premies are exposed to prolonged periods of IV nutrition. As a result, the mineralization of their bones is far from adequate to support normal growth and development. The treatment is supplementation with calcium, phosphorus, and vitamin D.

In general, over the relatively brief history of neonatology, the outcomes for premies have improved dramatically. This is true not only in terms of survival statistics, but in terms of survival with good function. One of the most famous premature babies in recent history was the first child of President and Mrs. Kennedy, in 1963. Patrick Bouvier Kennedy lived only thirty-nine hours. The He died of respiratory distress syndrome. The Kennedy baby was born at thirty-four weeks gestation. By the early twenty-first century, an infant born at thirty-four weeks has a ninety-nine percent chance of survival. This is because of advances including surfactant replacement therapy and high-frequency ventilation.

Preterm birth is very common. In 2011 in the US, almost twelve percent of all births were preterm. Of these, the subgroup that were extremely preterm was approximately six percent of the total. Prematurity is also a major source of the relatively high infant mortality rate in the US. Infants born at less than thirty-four weeks gestation comprise nearly sixty percent of all infant deaths.

Efforts to reduce premature birth have been succeeding. Between 2009 and 2012, the premature birthrate declined from twelve and a half to eleven and a half percent. The successes in this regard can be attributed to advances in technology and innovations over the last forty years. Our colleagues the anesthesiologists deserve their share of credit. The contributions of anesthesiology include rational intravenous fluid therapies, artificial airways and breathing circuits, as well as advances in mechanical ventilation. It is worth reiterating that Virginia Apgar was an anesthesiologist.

Survival among extremely low birthweight infants has increased dramatically over time. This has been the case for all gestational ages. Perhaps surprisingly, the improvement in survival over the decades has been sharpest for the twenty-four-week gestation group. In the nineteen eighties, the survival in this gestational age group was around ten percent. By the first decade of the twenty-first century, survival in the twenty-four-week gestation group was above sixty percent. The increases in the twenty-two and twenty-three-week gestation group are low, but have also increased over the last forty years.

Nevertheless, there is a fair amount of concern about long-term disability in NICU graduates. For infants born at twenty-five weeks, approximately half will leave the hospital with no major neurological disability. This is a stunning advance over previous decades. There is reason to believe that these trends will continue into the future. Nevertheless, the goal of perinatal medicine remains. As discussed early in this course, that goal is to limit prematurity as much as possible.

Key takeaways

- Premature infants need to remember to breathe on the own, eat on their own, and maintain their own body temperature.
- Respiratory distress syndrome results from surfactant deficiency; bronchopulmonary dysplasia is an iatrogenic disease resulting from respiratory support.
- Fragile premature brains suffer from intraventricular hemorrhage

- Patent ductus arteriosus can lead to congestive heart failure, so it is treated with indomethacin or surgical ligation.
- Jaundice of prematurity is very common and treated with intense blue light.

Quiz

1. Premies must be able to do three of the following things before they can go home. Which of the following is not one of them?
    a. Breathe on their own
    b. Feed on their own
    c. Poop on their own
    d. Regulate their body temperature on their own.

Answer c. Even if the premie needs assistance to make stool, she can go home.

2. At about how many weeks gestation (corrected) can a former premature infant accomplish the tasks needed to go home?
    a. thirty-four weeks
    b. thirty-five weeks
    c. thirty-six weeks
    d. thirty-seven weeks

Answer b. The true answer varies. For most normal prematures, by thirty-five weeks they can eat, breathe, and regulate their own body temperature.

3. Respiratory distress syndrome is not, strictly speaking, a syndrome. What is it?
    a. Relative pulmonary surfactant deficiency
    b. Relative pulmonary valve insufficiency
    c. Relative pulmonary pressure imbalance
    d. Relative pulmonary venous insufficiency

Answer a. A syndrome was defined in chapter two as a sequence of events, or as one event causing a number of disparate phenomena.

4. What kind of apnea is the apnea of prematurity?
    a. Obstructive apnea
    b. Central apnea
    c. Mixed apnea
    d. Post expulsive apnea

Answer b. The problem is a relative immaturity of the central respiratory center.

5. How many ounces does a third-trimester fetus gain per day?
    a. one half ounce per day
    b. fifteen grams per day
    c. ninety grams per day
    d. one ounce per day

Answer d.

6. What is the pathognomonic radiographic sign of necrotizing enterocolitis?

a. The halo sign

b. Kerley b lines

c. The train-track sign

d. Linear opacities

Answer c. This is the radiographic appearance of intermural air.

7. What is the most common bacterial species responsible for NICU infections?

    a. Streptococcus

    b. Staphylococcus

    c. Klebsiella

    d. Pseudomonas

Answer b. This is because of contamination with skin organisms. Klebsiella is second most common. Pseudomonas happens rarely. When it does, drastic decontamination measures are usually taken.

8. What is the cause of retinopathy of prematurity?

    a. Positive pressure ventilation

    b. Oxygen supplementation

    c. Premature exposure to light

    d. Excess intraocular pressure

Answer b. Like bronchopulmonary dysplasia, retinopathy of prematurity is an iatrogenic disease.

9. If bronchopulmonary dysplasia is not a dysplasia, then what is it?

a. A deformation

b. A malformation

c. A disruption

d. A displacement

Answer c. Malformations tend to be genetic or toxic metabolic in origin. Deformations tend to be caused by spatial constraints in the uterus. Displacements are not congenital anomalies.

10. All of the following are treatments for the osteopenia of prematurity except.

a. Folate

b. Calcium

c. Phosphorus

d. Vitamin D

Answer a.

Chapter seven: neonatal problems

We will now focus on the problems of full-term babies. Full-term patients in NICUs tend to be larger and sicker than their premature neighbors. Generally, a full-term infant will be admitted to a NICU because some untoward event has occurred, such as birth trauma. Sometimes the admission is planned, as when a prenatal diagnosis of a congenital anomaly has been made. We will discuss some of these in this chapter.

Respiratory distress is not a problem of premature infants alone. Although it is much rarer, grunting flaring and retracting can be seen in full-term newborns. The differential diagnosis is fairly broad. However, there are four major categories:

- Conditions relating to lung tissue
- Developmental abnormalities
- Mechanical abnormalities
- Airway abnormalities

Conditions relating to lung tissue include transient tachypnea of the newborn, discussed in an earlier section. This is retention of fetal lung fluid and resolves spontaneously hours after birth. Usually, only blow-by oxygen is used as therapy.

Meconium aspiration syndrome

The meconium aspiration syndrome deserves special mention here. The first meconium is not usually passed until after birth. However, in post-date babies, and some stressed fetuses, the first meconium is passed in utero. The first sign is usually dark green staining in the amniotic fluid. When meconium-stained fluid is seen, a pediatric team is summoned to the delivery.

The reason for this intervention is that meconium is toxic to lungs. It causes obstruction, hypoxia, and occasionally inflammatory pneumonia. To prevent this, the pediatric staff is called to suction any meconium present below the vocal cords before the newborn can aspirate it. When the baby is delivered, the attendant places a finger in the baby's mouth. This will inhibit the

baby's reflex to take a first breath. The baby is transferred to a warming table. There, an endotracheal tube is placed and suction is briefly applied. The presence of meconium below the cords is noted if present.

Despite these maneuvers, meconium aspiration syndrome cannot always be prevented. Treatment tends to be supportive, though surfactant is sometimes given. Some babies with meconium aspiration syndrome go on to develop reactive airways later in childhood.

Full-term respiratory distress syndrome

Respiratory distress syndrome occurs as well in the full-term infant. It is now believed that as many as seven percent of cases of respiratory distress in full-term newborns is caused by surfactant deficiency.

There are three types of full-term respiratory distress syndrome. The first is acute respiratory distress syndrome. This usually follows an event such as birth asphyxia or meconium aspiration. The second is idiopathic respiratory distress. This refers to babies delivered by elective cesarean section. There appears to be an inverse correlation with the gestational age at cesarean section and the incidence of idiopathic respiratory distress. The last form relates to genetic causes of surfactant deficiency. These are rare but associated with substantial morbidity and mortality.

The treatment of full-term respiratory distress syndrome depends on its severity. Because sepsis is a common cause of respiratory distress in newborns, empiric antibiotic treatment is prudent, especially in the initial stages. However, the most important intervention may be mechanical

ventilation. Continuous positive pressure ventilation is usually not adequate. Just as in preterm infants, full-term infants with respiratory distress syndrome should be treated with surfactant replacement therapy via the endotracheal tube.

In more severe cases, inhaled nitric oxide is an option. This gas has been shown to help reduce pulmonary vascular resistance, probably via smooth muscle relaxation. Because persistent peripheral hypertension is common in full-term respiratory distress syndrome, inhaled nitric oxide is a rational choice. Finally, the heart is often damaged as a consequence of this disorder, therefore, many centers administer prophylaxis against myocardial injury. This includes creatine phosphate sodium, sodium fructose diphosphate, and high-dose vitamin C.

Congenital pneumonia

Congenital pneumonia is generally the result of an ascending infection, or maternal chorioamnionitis. The diagnosis is made by chest x-ray (Figure Thirty-seven). This allows differentiation to be made from respiratory distress syndrome and other entities that will be described shortly. There are three types of congenital pneumonia: true congenital pneumonia, intrapartum pneumonia, and postnatal pneumonia.

True congenital pneumonia refers to the full-blown inflammatory process that is present at birth or shortly after birth. There are three sub-types of congenital pneumonia: hematogenous, ascending, and aspiration.

Hematogenous congenital pneumonia can occur if the mother is infected with a bloodstream-borne organism. Most organisms can cross the few layers of the placenta into the fetal circulation. Other causes include transient bacteremia that may follow from brushing teeth or even defecation. These situations are rare. More likely, hematogenous infection would occur if the mother is symptomatic with bacteremia. The infant is likely to develop systemic disease.

Ascending infection refers to organisms that cross into the fetal environment from the cervix. The amniotic fluid and membranes then become infected and inflamed. The birth canal and aspiration of infected or inflamed amniotic fluid have significant common features. Ascending infections may occur whether or not the membranes have ruptured.

Most ascending bacterial infections will be apparent in the mother. However, the infection may not be apparent if the membranes rupture shortly after the organism is introduced.

Once an organism is introduced into the amniotic fluid, the fetus is likely to aspirate it. Once this occurs, the organism needs to cross only the alveoli and the capillary endothelium to enter the bloodstream. Normally, newborns with pneumonia from ascending infections have more pulmonary than systemic signs.

Intrapartum pneumonia occurs as a result of organisms that are acquired from the birth canal. The route of entry may be hematogenous or may ascend. The infant may aspirate infected fluid. Alternatively, there may be mechanical disruption of a mucosal surface that has been freshly colonized with a maternal organism.

Postnatal pneumonia occurs during the first day of life. The mechanism may be identical to the those of hematogenous or ascending infections. However, the infection occurs after birth. The particular organism colonizes a mucoepithelial surface. Subsequently, some kind of barrier disruption allows the organism to ender the bloodstream, where it may seed the lungs.

Some of the risk factors for congenital pneumonia are iatrogenic. Broad-spectrum antibiotics are frequently used in obstetrics wards and in neonatal intensive care units. This practice predisposes the infant to colonization by organisms that are resistant and unusually pathogenetic. The invasive procedures that are often performed on these infants also allow microbes to breach physical barriers.

Aspiration may result from eating by mouth, leading to substantial inflammatory reactions. In addition, feeding tubes may further predispose infants to gastroesophageal reflux and aspiration.

The organisms

From the nineteen sixties to the late nineteen nineties, group B strep was the most common cause of congenital pneumonia. The late nineties saw widespread implementation of screening and treatment for group B strep. Though the incidence has decreased, it remains the most common cause of congenital bacterial pneumonia.

Other common organisms include:

- Non-typable Haemophilus influenzae

- Gram-negative bacilli
- Listeria monocytogenes
- Enterococci

Two important sexually-transmitted bacteria deserve mention here. Chlamydia trachomatis causes both pneumonia and conjunctivitis. The former condition tends to occur at about two weeks of life. Neisseria gonorrhoeae has also been reported as a cause of congenital pneumonia.

Empiric treatment of congenital pneumonia usually begins with broad-spectrum coverage including ampicillin and gentamicin. Serum levels of the latter must be measured because of its risks of nephrotoxicity.

Maternal chorioamnionitis

The issue of chorioamnionitis deserves some attention as it is a relatively frequent cause of neonatal infections.

The classic signs of chorioamnionitis are:

- Maternal fever
- Significant maternal tachycardia
- Fetal tachycardia
- Foul-smelling amniotic fluid
- Uterine tenderness
- Maternal elevated white blood cell count

If two or more of these signs are present, the newborn is at risk of becoming septic. Nevertheless, the signs we just listed may not be present in the context of chorioamnionitis. The infant, on the other hand, may exhibit symptoms. These include:

- General signs: hypotonia, weak cry, and weak suck
- Lung manifestations: tachypnea, cyanosis, respiratory distress, pulmonary hemorrhage, or apnea
- Cardiovascular manifestations: Tachycardia, hypotension, delayed capillary refill, clammy skin, pallor, or oliguria
- Gastrointestinal manifestations: vomiting, diarrhea, distention or bloody stools
- Central nervous system findings: temperature instability, behavioral abnormalities, apnea, or seizures
- Hematologic signs: petechiae or purpura, and overt bleeding

Treatment is the same as for congenital pneumonia. In asymptomatic infants, empiric therapy with ampicillin and gentamicin are continued until the infant's blood cultures are negative for forty-eight hours. If the infant has symptoms, treatment is continued for at least seven days.

Biographical sketch: Ignaz Semmelweiss

Semmelweiss is responsible for one of the most remarkable breakthroughs in the history of neonatology. Sadly, for Semmelweiss, the story does not have a happy ending.

Semmelweiss was born in Hungary in 1818. By 1844, Semmelweiss had completed his training and became an assistant at the obstetrics clinic in Vienna. Soon after, he became interested in what was called "puerperal fever", or "childbed fever" what we today call chorioamnionitis.

Whereas mothers usually delivered babies at home at that time, poor or homeless mothers delivered at the hospital. There, they would become deathly ill shortly after delivery and would often die. Their infants, too, often died soon after. The death rates approached numbers as high as thirty percent.

Dr. Semmelweiss's insight began with a simple observation. It turned out that there were two maternity wards in Vienna. One was staffed by midwives, and the other was a teaching ward, attended by teachers and their students. The death rate from childbed fever was two to three times higher on the teaching ward than on the midwife ward. Semmelweiss wondered if there was something about the physicians' hands that was the cause.

His suspicions began to solidify into a hypothesis when a friend and colleague died of a wound infection after examining a woman with childbed fever. It also turned out that the students would often examine laboring mothers immediately after having returned from performing autopsies in the adjacent morgue.

The germ theory of disease had not yet been promulgated, yet Semmelweiss determined that some agent must be present on the hands of the medical students. He ordered all the students to wash their hands in chlorinated lime water before examining the labor patients. In a very short period of time, the death rate from childbed fever fell from eighteen percent to one percent.

Though Semmelweiss's handwashing protocol was accepted in Hungary, it was rejected in Germany, which at the time was the center of the medical universe. The scientific revolution in

medicine was underway. In the absence of pathology that could be examined, the medical establishment refused to accept any medical idea.

This monumental rejection troubled Semmelweiss greatly. He sank into a deep depression, culminating in a nervous breakdown that saw him admitted to a psychiatric hospital. Semmelweiss was so badly beaten by guards upon his admission that he died two weeks later. The cause of death was sepsis, a darkly ironic ending to one of the greatest stories in the history of medicine.

Today, Ignaz Semmelweiss is hailed as a hero. In Budapest one may find a statue Dr. Semmelweiss standing above a grateful mother with her healthy baby.

Other conditions

Pulmonary edema, though rare is caused by increased pressure in the pulmonary microcirculation. It may be caused by birth asphyxia, respiratory distress syndrome, or patent ductus arteriosus. Treatment is aimed at eliminating the underlying cause.

Pulmonary hemorrhage is also rare in full-term newborns. When it does occur, it is most often associated with patent ductus arteriosus. Surfactant therapy is sometimes effective. Closure of the patent ductus is the definitive therapy. For other causes of pulmonary hemorrhage, the prognosis is very poor.

Congenital abnormalities of the lung

Developmental abnormalities causing neonatal respiratory distress in full-term babies are most often malformations. This means that the lungs fail to form normally.

Congenital lobar emphysema is also called congenital alveolar overdistention (Figure Thirty-eight) . It is characterized by one lobe of the lung failing to form terminal airways and alveoli. These lobes become hyperinflated after birth. The mass effect in the lung inhibits normal ventilation and perfusion of the lung. The result is hypoxia. The therapy is usually surgical removal of the emphysematic lobe.

Pulmonary sequestrations are segments of lung that are not attached to the pulmonary arterial blood supply (Figure Thirty-nine). As a result, this lung is said to be sequestered. It is also not connected to the normal airway tree. As a result, it does not contribute to lung function. Sequestrations often become infected and are therefore removed surgically.

Cystic adenomatoid malformation are similar to pulmonary sequestrations (Figure Forty). However, the causes and appearance are different. In cystic adenomatoid malformations, the entire lobe of a lung is replaced with a non-functional cyst. This space-occupying lesion can also interfere with normal oxygenation.

Tracheoesophageal fistula is another developmental anomaly. The esophagus and trachea separate during organogenesis. However, occasionally the separation is incomplete. After birth, swallowed liquid can be aspirated into the lungs. The infant may cough or be tachypneic. Aspiration pneumonia may result. The therapy is surgical ligation of the fistula.

Pulmonary hypoplasia was discussed during the section on congenital diaphragmatic hernia. However, hypoplasia may be caused by other anomalies already discussed. These include lobar emphysema, adenomatoid malformations, and sequestrations. There are all space-occupying lesions that interfere with the formation of normal lungs (Figure Forty-one).

Another important cause of pulmonary hypoplasia is oligohydramnios. It turns out that the fetal lung needs to breathe amniotic fluid in order to develop normally. In conditions of low fluid levels, the lung will become hypoplastic. The common endpoint of all these processes is that insufficient airway will be present in order to oxygenate the blood. Amniotic fluid transplants are possible but rarely performed.

We just discussed conditions relating to lung tissue and some developmental abnormalities. Now we will cover some airway anomalies that can give rise to respiratory distress in full-term infants.

Choanal atresia and choanal stenosis refers to incomplete development of the nose. As we discussed previously, newborns are obligate nose-breathers. This means they must breathe through their nose. The only way they can breathe through their mouths is to cry. One clue that a newborn may have choanal atresia is that the infant will cry often without other obvious reasons.

There are two other features of the nose that deserve mention. One is that the nose is the part of the respiratory system where the resistance to flow is the greatest. This is unfortunate for

humans, because the nose becomes narrowed with secretions so often. The other feature is a physical one: resistance to flow in a tube increases with the third power of the radius of the tube. For example, if the diameter of the tube is decreased by one half, the resistance in the tube increases two to the third power, or eight-fold. Therefore, even mild choanal stenosis can result in substantially increased work of breathing.

There is a simple test for choanal stenosis that can be performed in the nursery. A small catheter is introduced into each naris. If it cannot pass, choanal stenosis or atresia is suspected. The condition is corrected with surgery.

A laryngeal web is another airway anomaly that gives rise to respiratory distress. Also, a developmental anomaly, laryngeal webs develop from incomplete formation of the trachea. A mesh of tissue partially obstructs the trachea. As with choanal stenosis, a small amount of blockage can result in substantial resistance. The treatment is also surgical.

Laryngotracheomalacia occurs when the cartilaginous rings around the trachea fail to develop correctly. The upper airway becomes too soft, too narrow, or both. Upon inhalation, the trachea has tendency to collapse. This gives rise to the symptom called stridor. In most cases, the infant grows out of the condition. This is because the trachea becomes larger and stronger with time. In severe cases, tracheostomy is performed to bypass the region that collapses easily.

Subglottic stenosis is most often an iatrogenic disease. The phrase refers to narrowing of the area of the trachea just below the vocal folds. This narrowing is most often made of scar tissue caused by intubation. There is an idiopathic class of subglottic stenosis as well.

Having dealt with malformations and airway-related causes, we will finish the section on respiratory distress discussing mechanical abnormalities.

The rib cage of the newborn is more compliant than it will ever be during life. Compliance simply refers to the amount of pressure that is required to increase the volume of the space. More compliant spaces require less pressure to inflate. Despite its increased compliance, the rib cage must retain some stiffness, or will not ventilate properly. One rib cage anomaly that gives rise to neonatal respiratory distress is asphyxiating thoracic dystrophy, or Jeune syndrome. In Jeune syndrome, bones and cartilage fail to develop normally. The infant must breathe quickly and shallowly in order to maintain adequate ventilation of airspaces. Feeding by mouth is nearly impossible in severe cases, because of the increased work of breathing that feeding entails. Most patients with Jeune syndrome die from respiratory failure as babies or young children.

The air-leak syndromes also cause respiratory distress. The two important air-leak syndromes are pneumothorax and pneumomediastinum. Pneumothorax refers to presence of air in the pleural space. Pneumomediastinum refers to air in the spaces between the heart and the lungs. Most cases of pneumothorax in newborns occur spontaneously. Others occur as the result of excessive positive pressure ventilation. Small air leaks are usually asymptomatic. Larger ones will result in tachypnea, as the infant attempts to compensate for the ineffectively ventilating lung units. These

can be diagnosed by the presence of asymmetric breath sounds. Large air leaks are reduced by needling and suction until spontaneous healing.

Tension pneumothorax refers to air that enters the pleural space but does not escape. A ball-valve effect increases the volume of the air in the chest, crowding out healthy lung. Tension pneumothorax is easily relieved by needling. The respiratory distress diminishes immediately. Then the pneumothorax is reduced with suction until healing as with standard air leak syndromes.

Pleural effusions may be thought of as the cousin of air leak syndromes. Instead of air in the pleural space, fluid occupies the space, increasing work of breathing. Causes include heart failure, upper airway obstruction and pneumonia. Pleural effusions are drained the same way as air leak syndromes, with drainage, while the underlying cause is treated. A special case of pleural effusion is chylothorax. Chylothorax means lymphatic fluid that ends up in the pleural space. The causes in newborns are unknown. However, it can also result from trauma and surgery.

Jaundice revisited

Jaundice refers to the yellow color that results from the deposition of bilirubin in the skin. Bilirubin is a product of hemoglobin degradation and most often metabolized in the liver into a form that can be secreted in bile. The enzyme that catalyzes this reaction is immature in newborns. This is one reason why newborns are more prone to neonatal jaundice.

Another reason newborns are more predisposed to jaundice is that many of them are born with abnormally high hemoglobin content. This is called relative polycythemia. Excess numbers of blood cells are more likely to burst and release hemoglobin.

There are two major types of hyperbilirubinemia: conjugated and unconjugated. Conjugated, or direct, hyperbilirubinemia is the form that is made in the liver or conjugated. Bilirubin is conjugated with a molecule that permits clearance by the biliary system.

The conjugated hyperbilirubinemias have two types: hepatic and post-hepatic. Hepatic conjugated hyperbilirubinemia refers to causes that interfere with the ability of the liver to take up unconjugated bilirubin. These include infections such as hepatitis B, as well as inborn errors of metabolism such as galactosemia. Post-hepatic conjugated hyperbilirubinemia is most often caused by the congenital anomaly biliary atresia. In biliary atresia, some or all of the biliary tree fails to form. As a result, conjugated bilirubin backs up and ends up in the circulation, where it is deposited in skin. Biliary atresia is managed surgically.

Unconjugated hyperbilirubinemia is much more common. It can be divided in two parts, hemolytic unconjugated hyperbilirubinemia, and non-hemolytic unconjugated hyperbilirubinemia.

Of the hemolytic causes, there are two categories: intrinsic causes of hemolysis and extrinsic causes of hemolysis. Intrinsic causes have to do with defects inside the red blood cell. Extrinsic defects refer to causes outside the red blood cell.

The intrinsic causes of hemolysis can be divided into three subcategories: membrane conditions, enzyme conditions, and globin synthesis defects. Membrane conditions are genetic diseases in which the red blood cells do not form their usual bi-concave disc form. Spherocytosis is the best example. Spherical red blood cells are more rapidly captured and destroyed in the spleen and liver. Enzyme conditions include glucose-six-phosphate deficiency. Absence of these enzyme causes red blood cells to lyse in response to various toxic exposures. Globin synthesis defects like sickle cell anemia can also cause red blood cells to break, although this is less common in the early newborn period.

The extrinsic causes of hemolysis include the most common form, those related to antibodies. Hemolytic disease of the newborn refers to blood type incompatibilities. The most common of these is Rh disease. Rh-negative mothers make antibodies against their Rh-positive baby's red blood cells. Until the newborn clears maternal antibodies from their system, the condition persists. Another common cause of extrinsic hemolysis is sepsis.

The non-hemolytic causes of unconjugated hyperbilirubinemia are the most common. This is because one of these is breastfeeding jaundice. Breastfed babies are more likely to be jaundiced than are bottle-fed babies. This is because there is an enzyme in breast milk that inhibits hepatic uptake of bilirubin. Breastfeeding jaundice virtually never causes toxic hyperbilirubinemia in a healthy newborn. That is, unless the infant becomes ill, particularly with sepsis.

Other common non-hemolytic causes of jaundice include cephalohematoma, or a bruise on the baby's head from vacuum suction or forceps delivery. The extravasated red blood cells are broken down, releasing hemoglobin.

Congenital diaphragmatic hernia

Congenital diaphragmatic hernia is probably best described as a syndrome. That is because events occur in a sequence, beginning with an inciting event (Figure Forty-two).

The inciting event of congenital diaphragmatic hernia is a failure of developmental timing. During development of the intestines outside the abdomen, portions of the diaphragm close, separating the chest cavity from the abdominal cavity. In congenital diaphragmatic hernia, the closure occurs too late, or the intestines return to the body too soon. In either case, the returning intestines occupy both the abdominal and chest cavity. The presence of intestines in the chest has affects the growth the lung. This is almost always the left lung. However, because of the mass effect of the intestines, the contralateral, or right lung, may be hypoplastic as well.

At birth, respiratory distress occurs primarily as a result of insufficient lung formation. There may also be mass effect from the intestines. This mass effect would be particularly pronounced if the newborn swallows air during the initial crying after delivery.

The newborn may appear with a scaphoid abdomen, as the intestines that should be in the abdomen are in the chest instead. Bowel sounds may be heard in the chest, particularly on the left side. The heart will probably be displaced to the right. The point of maximum impact will be

displaced as well. X-ray usually confirms the finding. A nasogastric tube tends to be placed first, with suction to decompress the intestines. This is done prior to bag-mask ventilation. The reason for reversing the order of these procedures is that one does not want to introduce more air into the intestines. Doing so would worsen the respiratory distress.

Depending on the stability of the infant, the diaphragmatic defect is repaired surgically. The lungs may remain hypoplastic. However, they are likely to grow as the infant grows. Nevertheless, the prognosis may tend to be marked by restrictive lung disease. This means the presence of less total lung capacity than predicted.

A few other gastrointestinal problems of newborns deserve mention. By far the most common is gastroesophageal reflux. This topic was dealt with in some detail in a previous chapter. For our purposes here, it is enough to know two things: first, the gastroesophageal sphincter is much looser in newborns than in older children, so reflux is extremely common; second, the first treatment is angling the baby's body up thirty degrees.

Pyloric stenosis is a condition in which the muscular layer around the pyloric sphincter in the stomach becomes hypertrophic and does not relax properly. Pyloric stenosis is more common in boys, for unknown reasons. The cardinal sign of pyloric stenosis is projectile vomiting.

Now, most parents refer to any vomit that comes out of their child's mouth as projectile. However, true projectile vomiting is quantitatively and qualitatively different from spitting up. The strong newborn stomach is capable of expelling vomitus a distance of no fewer than five

feet. It is important for the clinician to ask the mother or caregiver how far the vomitus travels. Serum chemistries will also be disrupted. Because these infants expel hydrochloric acid, they will have metabolic alkalosis on blood testing. The treatment is laparoscopic incision of the pyloric sphincter. This is Heller's myotomy, and is usually curative.

The next important disorder of the gastrointestinal system affecting newborns is intestinal malrotation. During development, a fair amount of intestinal development occurs outside the body cavity. As the intestines return to the abdominal cavity, they must do so in a particular fashion that gives rise to the typical pattern. The colon should be fixed with the cecum on the right and the descending colon on the left.

If the process becomes disrupted, the intestines become susceptible to rotation about the mesenteric stalk. This is called mid-gut volvulus. This is a surgical emergency. The signs are bilious vomiting, distension, and sometimes shock when severe. Intestinal malrotation does not always occur at birth. It can occur later in infancy or even in childhood.

The last gastrointestinal obstruction we will cover here is Hirschsprung's disease. Hirschsprung's disease is a developmental failure of certain nerves to grow into the anal sphincter. As a result, the sphincter does not open reflexively with the descent of stool into the rectum. Stool accumulates in the colon, resulting in the occasionally fatal complication called toxic megacolon. The earliest sign of Hirschsprung's disease is failure to pass the first meconium. If this does not occur during the first two days of life, x-rays are taken. Definitive diagnosis is made by rectal

biopsy. The treatment is surgical excision of the denervated portion of the rectum, with pull-through and re-anastomosis.

Neonatal infections

As in most discussions of infectious diseases, we will divide neonatal infections into three sections, bacterial, viral, and fungal.

The two bacteria most commonly responsible for neonatal sepsis are group B *Streptococcus*, *Listeria monocytogenes*, and *E. coli*. As discussed in earlier sections, Group B strep is often acquired from the mother and can be a cause of late-developing sepsis. Similarly, *Listeria* can be acquired from tainted food and passed to the baby from the mother. The most common bacterial organism not transmitted vertically is *E. coli*. To empirically cover all three of these organisms in a sick newborn, both Ampicillin and Gentamicin are given.

Most of the viruses that cause disease in newborns are vertically-transmitted. Many of these were covered in previous sections. The most important non-vertically transmitted virus to remember is the respiratory syncytial virus, or RSV. In older children and adults, RSV is another of many causes of the common cold. However, in newborns, RSV is an important cause of bronchiolitis. Bronchiolitis is a small airways disease characterized by obstruction and excessive mucus secretions. The respiratory distress that results is a consequence of both the airways obstruction and the mucus secretions. In severe cases, apneas may occur, sometimes life-threatening. The care is usually supportive, with fluids. Respiratory support with mechanical ventilation is required in the most severe cases.

As in older children and adults, fungal infections are extremely rare unless the individual is immunocompromised. In premature infants, the most common invasive fungal infections are caused by *Candida* and *Aspergillus*. A completely benign candidal infection, thrush, is treated with oral nystatin.

We will leave infections now and turn to the endocrine system. The important case for newborns is that of the infant of the diabetic mother. This includes mothers with known gestational diabetes and those with undiagnosed gestational diabetes. As discussed in a previous chapter, diabetes in the mother can cause big babies or small babies. Large for dates babies develop as a result of exposure to excess circulating placental levels of glucose. Small babies develop as a result of small vessel damage in the placenta. This is seen most often in more severe and uncontrolled diabetic mothers.

Recall that the newborn's pancreas works perfectly well making insulin in response to whatever blood glucose level is available in placental blood. Infants of diabetic mothers have pancreatic beta cells that are revved up and pump out larger than normal amount of insulin to deal with the increased glucose load. As soon as the baby is born, they are suddenly detached from the increased levels of glucose. However, her pancreatic beta cells are still pumping out insulin. As a result, hypoglycemia ensues.

Neonatal hypoglycemia is characterized by jitteriness, hypotonia, and apathy. When severe, it can lead to seizures. The treatment is oral supplementation of five percent glucose solutions until the newborn's beta cells adjust to normal glucose levels in the blood.

There are a number of cardiac disorders that can affect the newborn. There are so many, in fact, that an entire course could be devoted to congenital heart defects. We will summarize the most important categories only.

Congenital heart defects

Congenital heart defects can be classified as hypoplastic, obstructive, septal, and cyanotic.

Hypoplastic defects, as the name implies, are developmental abnormalities in which one or the other ventricles fails to form correctly. Both left and right ventricular hypoplasia are ductal-dependent defects. This means that the newborn must have a patent ductus arteriosus, as well as a patent foramen ovale, to perfuse the body. This is why prostaglandin is such an important drug in newborn resuscitation.

The hypoplastic left heart syndrome refers to a sequence of developmental events (Figure Forty-three). Regardless of the underlying causes, the result is that the heart develops with a severely diminished left side. Most, or all the work of supplying blood to both the lungs and the body is performed by the right heart. For this reason, the maintenance of a patent ductus arteriosus is essential. If the duct were to close, the left side of the heart would be inadequate to provide adequate perfusion to the body. Shock and circulatory collapse would follow closely. This is why initial resuscitation must include infusion of prostaglandin, to maintain a patent ductus arteriosus.

While the ductus arteriosus remains patent, there is higher than normal resistance in the pulmonary circulation. This situation permits blood mixing in the atria. As a result, oxygenation may be adequate at birth, and the infant may appear normal. However, soon after, the ductus begins to close and resistance to flow to the lungs decreases. Flow through the ductus decreases dramatically while pulmonary flow increases dramatically. This diminishes delivery of oxygen to the systemic circulation.

Cyanosis and respiratory distress follow, progressing to shock. This type of shock is referred to as cardiogenic shock, named for its pathophysiologic origin. Initially, the newborn will be cyanotic and will not pink up with administration of oxygen. On occasion, the initial sign may be poor feeding. Alternatively, the extremities may become cool and pulses may begin to diminish.

The definitive therapy for hypoplastic left heart syndrome is surgery. These are always multi-stage procedures, generally performed over months to years.

The hypoplastic right syndrome may be easier to understand conceptually (Figure Forty-four). As the name implies, the right side of the heart is severely underdeveloped. As a result, it cannot pump blood adequately to the pulmonary circulation. Instead, blood flows right to left through an atrial septal defect. The mortality is very high in the perinatal period. As in the hypoplastic left heart syndrome, the two structures that keep these newborns alive are the ductus arteriosus and the foramen ovale. For this reason, in right-sided hypoplasia as well, prostaglandin is needed to prevent cardiogenic shock.

Obstructive defects refer to narrowing or stenosis of major vessels. The most common defects in this class are coarctation of the aorta, aortic stenosis, and pulmonic stenosis. When severe, all obstructive defects should be treated surgically.

Coarctation of the aorta refers to narrowing of this great vessel (Figure Forty-five). The most common form is the kind that concerns neonatologists. Here, the aorta is narrowed in the segment between the take offs to the arteries leading to the upper part of the body and the ductus arteriosus. This extremely high increase in resistance in the aorta results in decreased pressure in the vessel at the level of the ductus arteriosus. as a result, blood intended for the lungs will take a detour and head into the lower pressure descending aorta. The result of all of this is that infants born with coarctation of the aorta will have cyanotic lower extremities, but pink upper extremities. The treatment is surgical correction.

For reasons that are unclear, congenital coarctation of the aorta is associated with the genetic defect known as Turner syndrome. Turner syndrome is caused by the presence of only an X chromosome. These patients are phenotypically female.

Pulmonic stenosis is a key feature of the tetralogy of Fallot, which will be discussed in more detail shortly.

Septal defects refer to the muscular divide between the atria and the ventricles. The most common septal defects include patent foramen ovale and ventricular septal defects. As a group,

the ventricular septal defects are the most common form of congenital heart defect. They are most commonly detected by characteristic murmurs. The defects are considered hemodynamically significant when there are substantial amounts of left-to-right blood flow. The most severe cases are closed by endovascular patching or open-heart surgery.

Cyanotic defects are named accordingly because they result in bluish discoloration of the skin. This is the result of inadequate oxygenation of blood. The most notable defects are persistent truncus arteriosus, total anomalous pulmonary venous connection, the tetralogy of Fallot, transposition of the great arteries, and tricuspid atresia. All of these are indications for surgery.

The tetralogy of Fallot is the most common cause of cyanotic heart disease (Figure Forty-six). It accounts for about ten percent of total congenital heart defects. The tetralogy of Fallot is called as such because it is composed of four heart defects:

- Narrowing of the right ventricular outflow tract, including pulmonic stenosis
- Right ventricular hypertrophy
- Ventricular septal defect
- Aorta overriding the ventricular septal defect

These four defects may appear to be distinct. In fact, they all result from a single malformation in the course of heart development. This occurs early in the course of heart development. A structure called the conotruncal septum forms too far anteriorly, or closer to the chest wall. All

four defects follow from this developmental mistake. Some instructors refer to this syndrome as the monology of Fallot, in recognition of the importance of this single malformation.

Typical symptoms in newborns include generalized cyanosis. In addition, the odd sign called clubbing can occur. This is bulbous deformation of the tips of the fingers and toes, caused by chronic hypoxia. However, not all newborns are severely affected. Some may present initially with only feeding difficulties. Others may fail to thrive.

The classic presentation of the tetralogy of Fallot is the so-called "tet spell". These spells are episodes of cyanosis that can occur in the newborn period. These usually occur when the newborn becomes agitated. In such situations, the increased demand for cardiac blood flow gives rise to conditions of cyanosis. The treatment is keeping the newborn calm and giving supplemental oxygen.

The diagnosis is made by characteristic signs on echocardiography. Prenatal diagnosis via ultrasound is increasingly common.

The treatment is surgical, usually before the infant reaches one year of age. The ventricular septal defect is closed with a patch. The right ventricular outflow tract is enlarged.

Atrial septal defects

These defects are most commonly caused by failure of the foramen ovale to close at birth (Figure Forty-seven). The foramen ovale can be thought of as a pop-off valve. In fetal life, it allows

oxygenated blood entering the fetal heart to be pumped directly into the general fetal circulation. When this closure fails to occur after birth, blood shunts from the left atrium, where the pressure is higher, to the right atrium, where the pressure is lower. Since blood in the left atrium is already oxygenated, this defect does not result in deoxygenated blood ending up in the circulation.

On physical exam, the only finding may be a split second heart sound. This splitting occurs because the increased pressure in the overloaded right atrium causes the tricuspid valve to close after the mitral valve. Sometimes there is also a systolic murmur. It should be stressed that these are very difficult signs to detect on auscultation, particularly for new clinicians. The newborn heart rate can be one hundred twenty to one hundred sixty beats per minute. Very often these defects are not detected until adulthood. This may occur either incidentally in the course of an echocardiogram for other reasons. It may also occur in the course of a work-up for stroke. These details are beyond the scope of a course on neonatology. However, this neonatal condition affecting adult hearts is a substantial concern of internists, neurologists, and cardiologists.

Ventricular septal defects

In newborns, ventricular septal defects are the most common congenital anomalies. Because up to one half of these defects close spontaneously, the anomaly becomes substantially less common in adults.

There are two types of ventricular septal defect (Figure Forty-eight). The first is called a membranous defect. The second is called a muscular defect. These are named after the two

portions of the ventricular septum that fuse during development: the membranous and the muscular portion. Membranous defects are the more common of the two.

On a physiological level, what happens in a ventricular septal defect is that blood flows from the high pressure left ventricle into the low pressure right ventricle. As a result, oxygenated blood returns to the pulmonary circulation for another round of oxygenation.

In small ventricular septal defects, there may be no symptoms. There will, however, be a relatively high-pitched holosystolic murmur. This is relatively easy to hear in the newborn, even for the novice listener.

With larger ventricular septal defects, the increased left to right blood flow can cause pulmonary hypertension, leading to generalized increased pressure on the right. Over time, pressures on the right may exceed those on the left. When this occurs, shunting will occur in the opposite direction, or right to left. In order to prevent this outcome, surgical closure is recommended, often in the infant period. Closure can occur via open procedure or endoscopically, using patches.

Renal problems

Of the kidney problems affecting newborns, one of the most important anomaly was mentioned in the section on prenatal surgery. This is congenital ureteropelvic junction (UPJ) obstruction. Like pyloric stenosis, UPJ obstruction results from hypertrophic growth of the smooth muscle of the ureter. The back pressure of urine on the affected side can cause unilateral kidney failure.

Bartter syndrome is a rare inherited defect. It is characterized by low potassium levels and alkalosis. It is caused by a defect in the function of the kidney's filtering system in the glomerulus. Bartter syndrome is often suspected before birth, with the presence of polyhydramnios, or too much amniotic fluid. After birth, the infant drinks and urinates excessively, and is easily dehydrated. Bartter syndrome is usually treated medically with potassium supplementation and spironolactone to help prevent potassium loss.

Potter's sequence is the result of bilateral agenesis of the kidneys. The first sign of Potter's sequence is oligohydramnios, or too little amniotic fluid. Kidneys that do not form cannot make urine. The remainder of the signs in the sequence include pulmonary hypoplasia, club feet, and other deformations related to inadequate amniotic fluid. Potter's sequence is usually fatal or results frequently in early renal failure.

Sex development

Disorders of sex development are sometimes referred to as disorders of sex differentiation. There are a large number of these. We will focus on the three most important.

Congenital adrenal hyperplasia is caused by excessive androgen production by the adrenal glands. In genetic females, with two X chromosomes, this can lead to a masculinization of the female genitalia. The abnormally large clitoris can cause gender mis-assignment at birth.

Androgen insensitivity syndrome refers to genetically male babies who have defective androgen receptors. As a result, the genitalia develop with a female genotype. Androgen insensitivity syndrome is often not suspected until puberty, when affected individuals fail to menstruate.

Five alpha reductase deficiency refers to relative lack of the enzyme that turns testosterone precursors into active testosterone. In genetically male subjects, the individual appears female until puberty, when other testosterone-converting enzymes become active. Then the individual develops male secondary sexual characteristics.

Skin

Newborn skin disorders are interesting for an unexpected reason. All the common newborn skin disorders have terrifying, usually Latin names. Some of them even look terrifying. However, all of them are completely benign and resolve spontaneously without treatment.

Erythema toxicum neonatorum is not as toxic as it sounds (Figure Forty-nine). It is characterized by blotchy red spots on the skin with overlying whitish pustules. The cause is unknown. It appears during the first few days of life and can cover the entire body. The disappearance is dramatic, with all lesions vanishing in minutes to hours within the first two weeks of life.

Neonatal cephalic pustulosis, or baby acne, develops within two weeks (Figure Fifty). As mentioned in a previous chapter, baby acne results from withdrawal from maternal hormones. There is no treatment and it resolves by about two months of life.

Neonatal pustular melanosis is usually present at birth (Figure Fifty-one). It is characterized by whitish papules containing a milky exudate. They are usually wiped off in the delivery suite, leaving a hyperpigmented collar that soon disappears.

Milia is often confused with neonatal acne and occasionally with erythema toxicum (Figure Fifty-two). Milia tend to be whitish papules usually on the nose and sometimes the cheeks. Milia is completely benign and should not be treated.

Though the majority of skin disorders are benign. Some are not so benign. The lesions of herpes simplex are one such non-benign disorder. Herpes simplex virus can be passed to the fetus in utero (Figure Fifty-three). It may also be transmitted in the perinatal or postnatal periods. There are three primary syndromes associated with congenital herpes simplex. First is localized disease of the skin, eyes, and mouth. Second is involvement of the central nervous system with or without involvement of the skin, eyes, and mouth. Finally, there is disseminated herpes simplex infections, affecting numerous organs.

Localized herpes simplex in the face of the infant appears as small clusters of tiny vesicles surrounded by erythema. These progress to pustules and finally to crusts. In the eyes, the infant will tear excessively, and there may be conjunctival edema. Finally, in the mouth, there will be small localized ulcers as well.

The diagnosis of herpes simplex relies on detection of the virus. The Tzanck smear is the classic test derived from swabbed lesions. Immunofluorescence methods have also been used. The virus may be isolated by culture, or by detection of viral DNA by the polymerase chain reaction.

Unfortunately, these tests are not as sensitive as we need them to be. Negative testing, even with the polymerase chain reaction, cannot definitively rule out neonatal herpes simplex infection. If an infant is suspected of having central nervous system involvement, electroencephalography and other brain images should be performed. Early treatment is critical. Anti-viral medications can prevent the progress of skin, eye and mouth-limited herpes simplex to a more generalized infection.

Another less benign neonatal skin condition is Langerhans cell histiocytosis. This entity is a multi-system disease comprising a broad range of both benign and malignant presentations involving histiocytes. The presentation in infancy may resemble herpes simplex, atopic dermatitis, or benign nodules. For this reason, the diagnosis is frequently missed. In a patient with these skin manifestations that becomes seriously ill during the newborn period, skin biopsies should be performed. These will reveal histiocytes and may direct appropriate therapy. Steroids and other chemotherapeutic agents are typically used.

Seizures

We now move from the benign to the serious. Neonatal seizures are often serious events with poor prognoses. They can be classified in four groups, myoclonic, tonic, clonic, and benign.

Myoclonic seizures are not generalized and are not associated with electroencephalographic changes. They can be focal in one or many body parts and may be associated with severe encephalopathy.

Tonic seizures may occur in only one extremity or in the entire body. Focal tonic seizures that affect only one extremity are often measurable with electroencephalogram (or EEG). Generalized tonic seizures are characterized by extension of the upper and lower limbs. The majority are not measurable on EEG.

Clonic seizures are most often characterized by rhythmic movements with frequencies of one to three per second. They usually occur on only one extremity or one side of the body.

Benign newborn seizures typically occur around the fifth day of life. They are usually multifocal. the cerebrospinal fluid is normal. As the name implies, these are benign and resolve without treatment.

The treatment and prognosis of neonatal seizures depends on the cause. Hypoxic-ischemic encephalopathy and intracranial hemorrhage portend poor developmental outcome. similarly, genetic and metabolic disorders can have poor prognosis depending on the severity. Several dysplastic syndromes of the brain are characterized by seizures.

The treatments usually involve anti-seizure medications, used singly or in combination. The goal of therapy is to use the least amount of medication needed to prevent seizures. This is because

the medications carry side-effects that can affect development and function of the developing infant.

Perinatal stroke

The incidence rates for stroke peaks twice during the human lifetime. The most familiar peak is in the elderly. It is little known that the other peak incidence occurs in the newborn period. The phenomenon has only been discovered recently, with the advent of sophisticated brain imaging. Until recently, we were aware of the effects of apparent brain injuries in children, including hemiplegia, but we were unaware of the causes. Experts believe that neonatal strokes occur in one of every two thousand three hundred live births. This incidence is almost twenty times higher than that of children and young adults.

The signs of perinatal strokes tend to be non-specific. The infant may be hypotonic, apneic, or may suffer seizures. One oddity of the presentation is that these infants rarely present with asymmetric tone or movement, as do older children and adults. Newborn stroke victims that have seizures may appear and behave perfectly normally between seizures, different from the victims of hypoxic-ischemic encephalopathy.

Unless the affected neonate is born in a facility with advanced computed tomography or magnetic resonance imaging, they may be diagnosed later. Some patients are identified in the course of a work-up for developmental delay during the first year of life or even later.

It is often difficult to determine when perinatal strokes occur, but the expert consensus is that they can occur any time between week twenty-two of gestation and three days of life. Perinatal strokes may be in the differential diagnosis of birth asphyxia, discussed in an earlier chapter.

The sites of origin of these strokes are not well understood, but they have two general sources. The first is thrombosis of intracranial blood vessels. The other is embolism from either the placenta, the umbilical vein, the heart, or other extracranial sites.

A common outcome of perinatal strokes is cerebral palsy with hemiplegia. A diagnosis is sometimes not made until years after the event, in the course of a work-up of the condition. If the stroke was bilateral, the child may present with quadriplegia. The motor deficits are often accompanied by cognitive delays, behavioral problems, or seizures that do not respond to medical therapy.

Though the topic is beyond the scope of this course, it is worth mentioning that mothers too are at risk for stroke in the perinatal period. Thrombophilia is common in pregnancy, for complicated, probably multifactorial reasons.

Polycythemia, or high hematocrit, is a risk factor for stroke because of increased viscosity. This increased viscosity, combined with low flow in the placenta, create conditions amenable to formation of emboli. In fact, the placenta is probably underappreciated as a source of emboli. In a study of placentas from children with cerebral palsy, thrombotic lesions were the most common lesion found.

Birth trauma, in the form of traction on the newborn's neck, may predispose to thrombus formation. During the newborn period, especially for newborns admitted to the intensive care unit, relative dehydration and intravenous catheters may increase the risk of thrombus formation. In cases where the foramen ovale fails to close in a timely fashion, venous emboli may cross from right to left across the atrial septum. From there the thrombi may be thrown to the brain via the systemic circulation. Finally, maternal formation of anti-phospholipid antibodies may affect the placenta, resulting in formation of thromboembolism.

It is unclear whether perinatal strokes can be prevented. At present, the only known approach is to mitigate maternal risk factors such as smoking and obesity, both of which predispose to thrombotic events in the placenta.

Neural tube defects

Staying with the central nervous system, we will mention some important neural tube defects and one common endpoint of several conditions, namely hydrocephalus.

Neural tube defects originate very early in development, at about the third week of gestation. The cells that form brain and the spinal cord are supposed to generate a closed tube. When they do not do so, at either the brain or the spinal cord level, a neural tube defect develops.

The most common neural tube defect is spina bifida. Spina bifida has two forms, cystic and occult. Spina bifida cystica includes meningocele and meningomyelocele. These are herniations

of the meninges and/or spinal cord. In spina bifida occulta, the skin forms normally over the lower spine and no obvious defect is observed.

Spina bifida often results in paralysis below the affected area of the spinal cord. Bowel and bladder control are usually lost. Most children with spina bifida have normal intelligence, but some have cognitive delays. The deficits in spina bifida occulta are subtler and sometimes never become clinically significant.

Anencephaly is a rarer, but more severe neural tube defect, in which the forebrain and skull fail to form. These babies are usually stillborn or survive only a few days.

As mentioned in a previous chapter, folate supplementation, in the form of a prenatal vitamin, can reduce the incidence of neural tube defects.

Hydrocephalus

Hydrocephalus is one of the most common congenital anomalies, occurring in one in one thousand live births. It is characterized by enlargement of the ventricles and concomitant thinning of brain matter. It often follows severe hypoxic-ischemic insults. It can also follow from severe intraventricular hemorrhage, as discussed in the chapter on premature infants. Sometimes the cause is unknown.

The symptoms of hydrocephalus in the newborn are non-specific and can include:

- Poor feeding

- Irritability
- Less activity
- Vomiting

On physical exam, the affected newborn may have the following signs:

- Macrocephaly, with head circumference greater than the ninety-eighth percentile for age. Alternatively, there may be a rapid increase across percentiles on the head circumference curve. This is one reason why pediatricians measure head circumference at every well child visit.
- Non-junction of cranial sutures: These can be seen or palpated.
- Dilated scalp veins: The baby's scalp will appear thin and shiny and the veins will be easily visible.
- Firm fontanelle: When the calm infant is held erect, the anterior fontanelle may be excessively tense to palpation.
- Setting-sun sign: This is the pathognomonic sign of increased intracranial pressure in infants. The eyes deviate downward and the upper lids retract. The sclera, or whites of the eyes, are visible above the irises.
- Increased extremity tone: Spasticity is more common in the lower rather than the upper extremities. The reason for spasticity is stretching of the pyramidal tract fibers caused by the pressure from hydrocephalus.

In general, there are three mechanisms leading to excessive cerebrospinal fluid in the brain. These are overproduction, inadequate drainage, or impaired resorption of fluid. In some rare

cases, the cause is loss of brain tissue from some degenerative process. When this occurs, the increased space for fluid is a result not of too much fluid but of too little brain.

Benign external hydrocephalus is one example of too little absorption of cerebrospinal fluid. The intracranial pressure is slightly raised, and the subarachnoid spaces are abnormally large. This is thought to be a benign occurrence that resolves completely by the end of the first year of life.

The expression communicating hydrocephalus refers to instances in which there is no blockage to cerebrospinal fluid flow. However, there is overproduction or reduced absorption. Of these two, reduced absorption is far more common. Reduced absorption may occur in the context of intraventricular hemorrhage, as discussed in the chapter on the premature infant.

By contrast, non-communicating hydrocephalus refers to instances when flow is obstructed in the ventricular system or in the arachnoid space outlets. The result is reduced movement of cerebrospinal fluid the ventricles to the subarachnoid space. The most often encountered type of non-communicating hydrocephalus is obstructive. These are caused by space-occupying lesions.

Congenital hydrocephalus is most often caused by obstruction of the cerebral aqueduct. The two most common brain malformations giving rise to these obstructions are the Arnold-Chiari malformation and the Dandy-Walker malformation. The Arnold-Chiari malformation refers to herniation of the cerebellum through the foramen magnum. larger cerebellar vermian displacement. Hydrocephalus and other typical brain anomalies are well-known anatomic associations. The Dandy-Walker malformation is a more generalized malformation of the

cerebellum. As opposed to other forms of hydrocephalus in which the lateral ventricles are enlarged, in Dandy-Walker malformations, the fourth ventricle tends to be abnormally large. This is the ventricle that is located in the cerebellum.

Children with either of Arnold-Chiari or Dandy-Walker malformations may become stable in later childhood, but may suffer decompensations, especially after minor head injuries.

There is another, extremely rare, variant of congenital hydrocephalus that is worth mentioning. This is hydranencephaly, in which the cerebral hemispheres fail to develop to varying degrees. The remainder of the cranial cavity fills with cerebrospinal fluid.

Other congenital malformations leading to perinatal hydrocephalus include:

- Brainstem malformations that cause stenosis of the aqueduct of Sylvius: These cause ten percent of all newborn cases of hydrocephalus.
- Agenesis of the foramen of Monro
- Congenital toxoplasmosis, as discussed in the section on perinatal infections.
- The Bickers-Adams syndrome: An X-linked hydrocephalus accounting for 7% of cases in baby boys. It is characterized by stenosis of the aqueduct of Sylvius. Consequences include severe mental retardation. Half the children with this syndrome have a characteristic adduction-flexion deformity of the thumb.

The diagnosis is nearly always made by imaging. Head ultrasound can be performed at the bedside in the neonatal intensive care unit. For higher definition resolution of small structures, computed tomography or magnetic resonance imaging is employed.

The work-up in newborns also includes lumbar puncture, primarily for the purposes of measuring intracranial pressure. This is the so-called opening pressure, that can be measured at the bedside in the neonatal intensive care unit. The lumbar puncture needle can be placed in line with a sensitive pressure-measuring device.

Hydrocephalus is usually treated by shunting the fluid from the brain to the peritoneum. Medical therapy is introduced only as a delaying tactic while surgery is planned. Among other medications, the diuretic furosemide has been used to lower the quantity of cerebrospinal fluid production by the choroid plexus. Three quarters of all cases of hydrocephalus depend on shunts to avoid the consequences of increased intracranial pressure. In cases where obstruction is the cause, neurosurgery may be performed to alleviate the source of the obstruction.

Neonatal anemia

In an earlier chapter we discussed the anemia of prematurity. Here we will discuss anemia in more depth.

Anemia, or relative lack of red blood cells, particularly means lack of hemoglobin. Anemia can result from three general causes: lack of production, increased destruction, and sequestration of red blood cells.

Disorders leading to destruction of red blood cells are the most common. This is because they include the immune-mediated causes. Of the immune-mediated causes, blood type incompatibility is most common. Of blood type incompatibilities, Rh disease is by far the most common.

Rh disease is named after the rhesus monkeys in which the factor was first described. Rh incompatibility happens two ways: The most common type happens when an Rh-negative pregnant mother is exposed to Rh-positive fetal red blood cells because of hemorrhage. Such fetal-to maternal bleeding can occur during a spontaneous or induced abortion or from trauma. It can also result from invasive obstetric procedures, or even from normal delivery. The second cause of Rh incompatibility is triggered when an Rh-negative female receives an Rh-positive blood transfusion. This is extremely rare in the U.S.

The mother then produces antibodies to the Rh factor. These antibodies persist for life and may cross the placenta to the fetal circulation. There, they complex with Rh-positive fetal blood cells. This is a cause of fetal hemolytic anemia.

With each successive pregnancy in which there is an Rh-positive fetus, the risk and magnitude of the sensitization increases. For example, in mothers who are susceptible to Rh incompatibility, their second pregnancy with an Rh-positive fetus may give rise to an infant with mild anemia and jaundice. However, her subsequent pregnancies are likely to give rise to even more seriously

affected infants. In the worst-case scenario, the infants may die in utero from overwhelming antibody-induced hemolytic anemia.

Newborn hemolysis and jaundice can of course be treated; however, it is best to try and mitigate the effects of Rh-antibodies prior to birth. For Rh-negative mother, an anti-D immune globulin is given prenatally. It is best known as RhoGAM.

After delivery neonates with Rh incompatibility must sometimes be treated aggressively, depending on the degree of hemolysis that may already have occurred. Treatment depends on the newborn's red blood cell status, as well as overall cardiorespiratory status. Intensive phototherapy may be initiated. Emergent double volume exchange transfusion may be necessary. The latter has the effect of rapidly decreasing the quantity of circulating anti-Rh antibodies.

Since RhoGAM became commonly used in the United States, the risk of Rh disease has decreased from ten percent to less than one percent. RhoGAM is given to the mother by injection around thirty weeks gestation and again within three hours after birth.

Affected newborns often become jaundiced on the first day of life. The treatment is with phototherapy, as described in the chapter on NICU care. These newborns do not need to be transferred to the NICU. They can be treated in the well-baby nursery, or even at home. Rh disease is transient and recovers quickly.

At this point, we should mention the haptoglobin test. Haptoglobin is a circulating protein that binds free hemoglobin. When hemoglobin levels drop because of hemolysis, haptoglobin is consumed in the process of binding hemoglobin. Haptoglobin levels will be zero or near zero in hemolytic conditions. Thus, the haptoglobin test aids in determining the differential diagnosis of anemia in the newborn.

The other causes of increased destruction of red cells were discussed in the section on jaundice. Briefly to review, they are membrane disorders such as spherocytosis. There are also the hemoglobinopathies, of which sickle cell disease is the most prominent. Loss through bleeding or intense bruising is usually obvious on presentation. Sequestration of red blood cells, as in the spleen, is extremely rare.

Decreased production of red blood cells include conditions that are also particular to neonatology. These anemias are described generically as aplastic anemias. This is because they are characterized by lack of production. Of the congenital aplastic anemias, the most notable is Diamond-Blackfan anemia. Named after two of its discoverers, Diamond-Blackfan anemia involves an arrest in the development of the erythroid line of bone marrow cells. The infant becomes progressively anemic as previously developed red cells are destroyed. Treatment with steroids can help revive the stalled bone marrow.

Polycythemia, or excess of red blood cells, was discussed in the section on jaundice as well. This is a result usually of excessive transfer of blood from the placenta to the fetus, usually at the time of birth. It can also result from a twin-twin transfusion. The newborn appears beet red, a

condition known as plethora. Usually, plethora is not a problem. With excessive polycythemia, however, the blood can become so viscous as to create thrombotic conditions. Thrombosis in the newborn will be discussed shortly. In these cases, selective bleeding is performed to return hemoglobin levels to closer to normal levels.

Coagulation disorders

As mentioned, the coagulation disorders are rare, but they merit mention. One of these disorders, hemorrhagic disease of the newborn, is now vanishingly rare because vitamin K is typically given at birth. Vitamin K is a cofactor for a number of clotting factors. For reasons that do not make a great deal of evolutionary sense, levels of vitamin K are low in newborns. In addition, breast milk is low in vitamin K. Other coagulation disorders worth mentions include deficiencies of protein C and protein S. These levels are measured in the course of a work-up for anemia in the newborn.

Neutrophil dysfunction

Disorders of neutrophil function or number will be discussed here. The important point to mention is that there is a particular sign in the newborn that signals neutrophil disorders. This is delayed separation of the umbilical stump. As soon as the infant is born, the immune system begins to recognize the umbilical stump as foreign. The process of rejection begins. Normally, the umbilical stump falls of in two to four days. If the cord has not fallen off in two weeks, neutrophil abnormalities should be suspected. These are worked-up initially with complete blood counts.

Primary immunodeficiencies

These disorders, though rare, can appear during the newborn period. Congenital immunodeficiencies are genetic in nature. They are differentiated from secondary, or acquired immunodeficiencies, such as AIDS. Approximately one in five hundred people are born with a primary immune deficiency, some more severe than others. Primary immunodeficiencies can cause persistent or recurring infections, inflammatory disorders, and even tumors. With the exception of bone marrow transplant, these diseases are incurable.

One of the most important, though rare, primary immunodeficiencies is the severe combined immunodeficiency, or SCID. In SCID, there is a functional loss of both T and B cells. The two main types of SCID are X-linked severe combined immunodeficiency and adenosine deaminase deficiency. The X-linked form is the result of mutations in the common gamma chain. Adenosine deaminase is responsible for breakdown of purines. In the absence of the enzyme, a cascade of developmental errors occurs culminating in failure of lymphocyte development.

Newborns with SCID suffer severe bacterial, viral, or fungal infections. They often have interstitial lung disease, chronic diarrhea, and failure to thrive. In addition, from a very early age they suffer from ear infections, and pneumonia from opportunistic pathogens. Most of these infants have severe oral thrush. Left untreated, these babies will die within one year. The treatment is hematopoietic stem cell transplant.

DiGeorge syndrome deserves mention here. This is a genetic disease that gives rise to several seemingly disparate congenital anomalies. This syndrome has been associated with deletions of

part of chromosome twenty-two. In addition to an immune deficiency, babies born with DiGeorge syndrome have congenital heart defects, and characteristic facial features. They are often developmentally delayed and may have cleft palate. Other conditions often associated with the syndrome are kidney problems, and hearing loss. One of the characteristic signs that may raise the index of suspicion for DiGeorge syndrome is absent or hypoplastic thymus. On newborn x-rays, the thymus is often large, covering much of the upper mediastinum. In the course of a work-up for cardiac anomalies, absence of thymic shadow is an indication for genetic testing.

The floppy baby

We will now discuss a condition for which the neonatologist is often consulted in the newborn nursery, the hypotonic infant. Hypotonia in newborns has a number of causes, many of which are beyond the scope of this course. However, it is important to recognize the several categories of disorder that can give rise to a floppy newborn. These are:

- Anterior horn cell disorders, particularly spinal muscular atrophy.
- Neuromuscular junction disorders, particularly congenital myasthenia, discussed in an earlier section.
- Congenital myopathies
- Muscular dystrophies. These do not include classic Duchenne muscular dystrophy, whose symptoms do not appear until the toddler years.
- Metabolic and multisystem diseases, particularly some of the inborn errors of metabolism discussed in earlier chapters.
- Congenital motor or sensory neuropathies

Only one type of spinal muscular atrophy is present at birth. This is the most severe subtype, spinal muscular atrophy type one. It is also called Werdnig–Hoffmann disease. The disorder is characterized by loss of motor neurons and muscular wasting. It is an autosomal recessive disorder with very rare incidence. Spinal muscular atrophy is the most common genetic cause of infant death. The clinical signs are a floppy, or hypotonic baby.

Congenital myopathies are a group of disorders of muscle development and function. The annual incidence is approximately six in one hundred thousand live births. The most common is nemaline myopathy. Nemaline myopathy is characterized by generalized low muscle tone and weakness. Affected infants often die in the newborn period. None of the congenital myopathies are treatable at present. Length of survival depends mainly on the integrity of respiratory muscles.

The muscular dystrophies and congenital motor and sensory neuropathies are generally not present during the newborn period.

Thrombosis

Neonatal thrombosis is a condition that primarily affects patients admitted to the neonatal intensive care unit. As is the case with adult patients, the majority of these cases occur as a result of thrombus formation on indwelling catheters.

An unusual site of thrombosis deserves mention because it is particular to the sick neonate. The practice of umbilical vein catheterization has led to an increased incidence of portal vein thromboses. As discussed in a previous section, complex congenital heart disease is common in the neonatal intensive care unit. The turbulent flows associated with these malformations, both uncorrected and corrected, can create conditions for thrombus formation.

Diagnosis of thromboembolism is highly dependent on the location of the blockage. Portal vein thromboses often present as splenomegaly and even bloody stools. Ultrasound and angiography, in experienced hands, can help in location of emboli.

Treatment is fraught with the balance between risk of further embolus formation and risk of hemorrhage, as is the case with adults. Fractionated heparin has been used, as has been recombinant tissue plasminogen inhibitor.

Bones and joints

The most important congenital bone malformation is arthrogryposis. The name derives from the Greek words meaning “curved bones”. Arthrogryposis is a genetic disorder with a wide spectrum of presentation, from mild to widespread and severe. The therapies often involve surgical reconstruction of the affected bones and joints.

Club foot, or talipes equinus, is the most important sub-category of arthrogryposis. As discussed in a previous section, club foot can also be a deformation resulting from oligohydramnios. This condition is sometimes familial and is corrected with surgery.

Osteogenesis imperfecta, as its Latin name implies, is a defect in bone generation. The four types of osteogenesis imperfecta are all related to genetic defects in collagen production. Newborns with the more severe type of osteogenesis imperfecta often present at birth with multiple broken bones. This can even occur during the process of delivery. Patients with osteogenesis imperfecta do not grow normally because of the collagen defect. They undergo countless surgeries to pin and otherwise fix their numerous broken bones.

Hearing and vision

Most causes of congenital deafness are genetic, either autosomal or recessive. Treatment relies heavily on early intervention, to teach the child non-verbal communication skills. Some of the causes of congenital deafness are treatable with hearing aids or cochlear implants. Of the causes of neonatal blindness, the most important was already discussed, retinopathy of prematurity. Recall that retinopathy of prematurity is an iatrogenic disorder, caused by exposure to oxygen. There are also genetic and infectious causes of neonatal blindness.

Key takeaways

- Respiratory distress may be caused by malformations, deformations, or mechanical disruptions of the chest wall and upper airway.

- Jaundice is caused by a combination of excess production and decreased metabolism of bilirubin. Jaundice is treated with phototherapy.
- Group B strep is the most common cause of neonatal sepsis, followed by *E. coli* and *Listeria*.
- The physiology of the ductus arteriosus is important for understanding management of the newborn with congenital cardiac disorders.

Quiz

1. Which of the following is a pulmonary malformation?
    a. Congenital diaphragmatic hernia
    b. Congenital lobar emphysema
    c. Congenital pleural effusion
    d. Congenital surfactant deficiency

Answer b. The others are causes of newborn respiratory distress, but they are not congenital malformations.

2. Why do upper airway disorders cause respiratory distress?
    a. Floppy or narrow tubes collapse when flow increases in them.
    b. The trachea requires cartilage in order to form a tube.
    c. Tracheal intubation always damages the subglottic area.
    d. Newborns are obligate nose-breathers.

Answer a. The trachea does not require cartilage to form. Tracheal intubation sometimes, but not always causes subglottic stenosis. Newborns are obligate nose breathers, but this is not why upper airway problems cause respiratory distress. Breathing by mouth does not alleviate the problem.

3. All of the following are bacterial causes of neonatal infection except:
    a. Group B strep
    b. Listeria myocytogenes
    c. Escherichia coli
    d. Streptococcus pyogenes

Answer d. This is the causative agent of strep throat, among other infections.

4. All of the following are part of the initial management of congenital diaphragmatic hernia except:
    a. Bag-mask ventilation
    b. Nasogastric suction
    c. X-ray
    d. Observation of scaphoid abdomen

Answer a. Until intestinal suction is achieved bag-mask ventilation is contraindicated. This is because positive pressure ventilation can inadvertently inflate the intestines, worsening the gas exchange in the already compromised lungs.

5. Which of the following gastrointestinal system disorders is correctable by laparoscopic surgery?
    a. Intestinal malrotation with midgut volvulus
    b. Hirschsprung's disease
    c. Pyloric stenosis
    d. Congenital diaphragmatic hernia

Answer c. Heller's myotomy is a relatively simple laparoscopic procedure. The others require open laparotomies.

6. Which congenital heart defects require prostaglandin therapy?
    a. Atrial septal defects
    b. Ductal-dependent defects
    c. Ventricular septal defects
    d. Obstructive defects

Answer b.

7. Which of the following newborn signs is characteristic of upper airway obstruction?
    a. Stridor
    b. Wheezing
    c. Grunting
    d. Retracting

Answer a. Wheezing, grunting and retracting are signs of distress, but they are not characteristics of upper airway obstruction

8. Which of the following causes of neonatal anemia is caused by defects in red cell membranes?
    a. Congenital myasthenia
    b. Congenital spherocytosis
    c. Sickle cell disease
    d. Diamond-Blackfan anemia

Answer b. Spherical erythrocytes are more likely to be cleared by the spleen. Myasthenia is an extrinsic immune cause of anemia. Sickle cell disease is a hemoglobinopathy. Diamond-Blackfan anemia is a defect in red cell production.

9. What vitamin helps reduce the incidence of neural tube defects?
    a. Niacin
    b. Riboflavin
    c. Folate
    d. Thiamine

Answer c.

10. Which of the following disorders of sex development is often discovered when an adolescent female fails to menstruate?
    a. Congenital adrenal hyperplasia
    b. Five alpha reductase deficiency
    c. Androgen insensitivity syndrome

d. Ambiguous genitalia syndrome

Answer c. These children are genetically male but phenotypically female.

Chapter eight: Care in the neonatal intensive care unit

In this final chapter of the course we will deal with some aspects of the neonatal intensive care unit that were not covered in the previous chapters. We will specifically talk about pain management and issues related to neonatal pharmacology. We will also briefly discuss efforts made in NICUs to improve quality of care and reduce critical incidents. Both of these topics are related to the concepts of evidence-based medicine and medical ethics. As most NICUs are located in academic medical centers, a fair amount of research takes place there. We will briefly review issues related to research and informed consent. Since prematurity and other neonatal diseases carry substantial mortality, NICUs also provide palliative and end-of-life care. Some of these issues will be discuss. Finally, we will discuss the babies who leave the NICU and are followed up after discharge.

For much of the history of pediatrics, the consensus was that fetuses and, by extension, premature infants did not feel pain. It was thought that noxious stimuli were not registered in the newborn cortex as pain. The withdrawal reflexes in response to painful procedures were considered reflexive. Needless to say, there was no scientific basis for this conclusion. Once it was acknowledged that neonatal pain was indeed a real phenomenon, dosing pain medication remained a problem. The fear was that extrapolating adult doses of pain medication to children

might result in overdoses. To the contrary, in the early days of neonatal pain management, pain was likely undertreated, rather than over-treated.

An obvious problem in neonatal pain management is that the patients cannot communicate. This problem was circumvented by the development of pain scales, integrating facial reactions, body movements, and changes in vital signs.

The choice of pain medication is also problematic in neonates, especially in premature infants. Under the best of circumstances, pharmacokinetics in sick patients are determined on the basis of trial and error. This is because studies are difficult to perform for various reasons, including consent issues. Nevertheless, attempts have been made to determine appropriate dosing of medication based on weight.

The most commonly used medications for pain relief in the NICU are acetaminophen and ibuprofen. Intravenous ketorolac, another nonsteroidal anti-inflammatory, is also frequently used. For pain control during brief painful procedures, administration of five percent glucose has been attempted. There is some preliminary evidence that the immature fetal brain responds to glucose as a kind of anesthetic. The details of the phenomenon are not well-understood.

Opioid use is also problematic in neonates for a variety of reasons. Chief among them is that some neonates experience a reaction to opioids that is not observed in other patients. This is chest wall rigidity. For obvious reasons, this is an undesirable side-effect in patients with

respiratory distress. The mechanism of chest wall rigidity is unknown. It is reversed with naloxone.

In addition, there are occasional opioid overdoses in the NICU. These occur because it is not always possible to determine an individual patient's ability to metabolize opioids. NICU staff are prepared at all times to monitor for signs of respiratory depression, and to reverse them with naloxone if necessary.

The specific problem of managing pain in the NICU is related to the general problem of neonatal pharmacology. Drugs behave differently in neonates. As a result, one cannot extrapolate doses and pharmacokinetic profiles even from older children. Therefore, pharmacological data can only be obtained from clinical trials in neonates. For reasons we will discuss shortly, such trials are difficult to perform.

Serious side-effects in newborns have been noted since the 1950s. Early in the history of neonatology, it was discovered that sulfonamide antibiotics caused hyperbilirubinemia. The antibiotic chloramphenicol became associated with aplastic anemia. Even the saline used to flush IV catheters was implicated in adverse reactions. Toxic doses of benzyl alcohol were found in saline, associated in particular with vitamin E preparations.

Intensive care units in general, and neonatal intensive care units in particular, are cognizant of quality improvement. In the recent past, NICUs had been places where adverse events frequently occurred, resulting in a fair amount of morbidity and mortality. Premature infants

were resuscitated, but often suffered long-term complications. These included cognitive and physical disabilities. In addition, the treatments themselves carried risks of adverse events. We have already discussed two examples of iatrogenic damage, bronchopulmonary dysplasia and the retinopathy of prematurity.

As a result of this history, as well as for other reasons, most NICUs associated with academic medical centers engage in robust quality improvement programs. One key to reducing the incidence of untoward events and accidents was recently developed. The key was to report all events, including inconsequential events. In this context, the term inconsequential means that the patient did not suffer any adverse outcome. However, by documenting and tabulating all such events, quality improvement teams can address not only the small events, but also the significant ones that result in patient harm. The movement to reduce patient harm, especially referring to side-effects of treatments, has been gathering steam in recent years.

Currently, virtually all procedures and treatments are subjected to quality improvement review. If enough data are collected to suggest that a procedure or treatment provides no benefit, they are discontinued. This is of course the case for procedures and treatments that are found to be more harmful than helpful. In general, anonymous, voluntary, non-punitive reporting methods reduced harms to the greatest extent. The non-punitive nature is the most important aspect in this regard.

By far, the most common errors leading to critical events are medication errors. These can result from improper dosing, frequency, or administration. The true incidence of these events is not known. This is because there is good evidence to suggest that critical events are underreported.

Other industries such as manufacturing have successfully managed the problem of underreporting. There are several reasons why underreporting happens in medicine, including the fear of litigation.

The scientific study of medical errors has been tied to the recent trend of evidence-based medicine. Evidence-based medicine has been defined as the use of credible scientific evidence in decision-making. A problem with evidence-based medicine emerged almost as soon as the concept began to be adopted. The problem was that patients, specifically the patients parents, bring their own beliefs and values to a decision-making process. Parental desires often conflict with the findings of evidence-based medicine.

When decision-making regards life-or-death situations, the problem becomes even more complicated. There are rare cases in which evidence basis favors a life-saving therapy, but the parents refuse that therapy. In these cases, the state, or legal systems step in which only complicates the process.

Having stated all this, there is one major feature of evidence-based medicine that must be stressed. That is, there is far more about outcomes that is unknown than is known. In other words, the volume of evidence-based medicine is much smaller than the public imagines. Decisions made in the NICU in particular are often made based on personal experience and clinical judgment, rather than on an evidence basis. For this reason, it is imperative that care givers practice good ethics.

In the public mind, physicians know a great deal more than they actually do. The truth is that there is a great deal of uncertainty in the treatment of a neonate. Good ethics requires, first and foremost, telling the truth. One of the hardest things for a physician to do is to admit that they do not know the answers. Nevertheless, one thing that neonatologists should never do is make statements and recommendations based on non-existent knowledge.

A good example is the question of neonatal pain that we discussed earlier in the chapter. For a long time, physicians told parents that premature babies were unable to experience pain. The truth was that physicians did not know whether premature babies could experience pain. The result, in the case of neonates, is that generations of small babies endured substantial pain during treatment. Treatment of pain has vastly improved. It is unclear if managing uncertainty on the part of physicians has improved.

Another aspect of good ethics is describing to parents what is known and what is not known. This aspect becomes particularly important when research projects are underway.

It is a commonplace that knowledge in any field of medicine cannot increase if research is not conducted. Nevertheless, since the seventeenth century, the scientific method has been the accepted mode of advancing knowledge. However, when research is to be conducted in the NICU additional problems are encountered.

One problem involves the granting of consent. Informed written consent laws vary by state. Nevertheless, there are several commonalities. A physician has a general responsibility to give

information to parents in such a way that they can make a reasonable decision. The physician needs to list all the possible risks and benefits. Alternatives must be presented as well. Finally, the parent must signal agreement in writing.

The problem is that consent for participation in studies must be obtained from parents. Many parents of fragile newborns are less likely to consent to participate in studies. One of the reasons is that the decision-making process involves a person other than the individual offering consent. It is often easier to consent to participate when one would participate oneself. Another reason is that parents appropriately consider newborns to be worthy of particular caution. This is especially true of the tiniest premature infants.

For these and other reasons, research studies are difficult to perform in NICUs. In order to reach statistical significance, substantial numbers of subjects are needed. This is especially true for studies that are expected to reveal only small changes. Research in NICUs are most successful when they include more than one center, with many patients, over relatively long periods of time.

Not all treatment is successful. In neonatology, as in any other branch of medicine, some patients are transitioned to palliative care. Much of the time, it is difficult to know when therapy will no longer provide a benefit. For these and other reasons, the reason to switch to palliative therapy, or to discontinue therapy, is often delayed in the NICU.

For some conditions, early death is common. Examples include anencephaly, as discussed in a previous chapter. In such cases, efforts are made only to make the patient as comfortable as

possible. Invasive procedures such as insertion of central catheters are avoided. Instead, fluids and opioid medications are given, by mouth if possible. Parents are given maximum time to spend with their baby.

Cases where patients are extubated are particularly difficult. By the time a decision to extubate is made and agreed upon, the caregiving team has usually known for some time that the infant is extremely unlikely to survive. This is especially the case for micro-premies in whom multiple organ damage occurs, particularly brain damage. In some cases of older premature infants, efforts to wean respiratory support repeatedly fail over long periods of time. In these cases, when parents and staff reach consensus that recovery is virtually impossible, arrangements are made to extubate the patient. As described above, there is generous use of opioid medication, in order to reduce the infant's distress to the greatest extent possible.

When babies die, they are treated with the utmost respect, as would be afforded to an older child or adult. Depending on the faith community the family belongs to, the infant may be baptized or otherwise named officially. One custom typical of NICUs deserves mention. Inked footprints are imprinted on cards for the parents to keep as memorials. The bodies are handled and transferred to funeral homes as are older patients.

Happily, for NICUs, most babies are discharged healthy. As we discussed in an earlier chapter, an infant must be able to do three things prior to going home: breathe on their own, eat on their own, and regulate their body temperature. We mentioned in various places that thirty-five weeks, corrected, is often the age at which healthy premature infants accomplish these tasks. However,

this is not always the case because of intercurrent events such as weight loss. Therefore, most NICU staff advise parents that a rough estimate of discharge date will be around the baby's due date. Nevertheless, the best advice is that the patient can go home after accomplishing the three tasks.

As difficult as research is for acutely ill patients, it is that much easier in NICU graduates. Not surprisingly, there is a substantial amount of published data regarding outcomes of NICU graduates. Typically, a NICU graduate will attend regular clinic visits in order to track growth and development. In addition, recovery from conditions such as retinopathy of prematurity are tracked closely. This is done to retrospectively determine what treatments are most likely to reduce the condition. Retrospective studies are by far more common than prospective studies, for this reason.

Key takeaways

- Premature infants feel pain.
- Dosing medications must respect the particularities of sick premature infants.
- Quality improvement is best accomplished by multi-center, anonymous, voluntary, non-punitive reporting systems.
- More is unknown than is known in neonatology.
- Most patients admitted to NICUs are discharged home healthy.

Quiz

1. Which of the following pain medications are not used in the NICU?
    a. Morphine
    b. Fentanyl
    c. Acetaminophen
    d. Chloramphenicol

Answer d. Morphine and fentanyl are opioids. Chloramphenicol is an antibiotic, no longer used in infants.

2. At what age do premature infants feel pain?
    a. Twenty-four weeks
    b. Twenty-five weeks
    c. No premature infants feel pain
    d. All premature infants feel pain

Answer d.

3. The most effective quality improvement programs do which of the following?
    a. Measure outcomes
    b. Measure all untoward events
    c. Measure prevalence of outcomes
    d. Measure incidence of legally-actionable events

Answer b. The best programs measure all events, even if they do not result in bad outcomes.

4. The most effective quality improvement programs are all the following except:
    a. voluntary
    b. anonymous
    c. reportable
    d. non-punitive

Answer c. All events are reported in the best programs. The feature of the best programs not mentioned are multi-center programs

5. Which of the following is true about evidence-based medicine?
    a. Most treatments in medicine are evidence based.
    b. More is unknown than is known.
    c. All treatments and procedures in the NICU become part of the evidence base.
    d. Only evidence-based treatments are subject to informed consent requirements

Answer b. More is unknown than is known. Most things that happen in NICUs do not add to the evidence base. All procedures and treatments require informed consent.

6. When is palliative care offered?
    a. When supportive therapy is not available.
    b. When the parents refuse consent.
    c. When curative therapy is not supported by the evidence base.
    d. When there is no evidence basis for any therapy.

Answer a. This is the case for anencephalic infants, as well as many other disorders.

7. Which of the following is not permitted to go home with the infant?
    a. Supplemental oxygen
    b. Nasogastric tubes
    c. Monitors
    d. Mechanical ventilators

Answer d. Oxygen, nasogastric feeds, and monitors are all used at home to allow the infant to be discharged.

8. Which of the following do not require informed written consent?
    a. Antibiotic therapy
    b. Oxygen therapy
    c. Neither a nor b
    d. Both a and b

Answer d. Standard cares such as antibiotics and oxygen are covered by the standard consent form signed upon admission to the NICU.

9. Which condition is a subject of NICU follow-up?
    a. Retinopathy of prematurity
    b. Sickle cell disease
    c. Phenylketonuria
    d. Transient tachypnea of the newborn

Answer a. Sickle cell disease and phenylketonuria are not particular concerns of the NICU. Transient tachypnea of the newborn is generally not treated in the NICU

10. When are former premature infants discharged from the NICU?

    a. On their due dates
    b. When they achieve thirty-five weeks gestation, corrected
    c. When they no longer require oxygen
    d. When they can breathe, eat, and regulate body temperature on their own.

Answer d. The exception may be babies that are exclusively tube fed, including those fed by gastrostomy tube.

Conclusion

Neonatology is one of the newest subspecialties of pediatrics, that is itself a subspecialty of internal medicine. As such, neonatology is one of the newest major specialties in medicine. It is also one of the most successful branches of medicine. Neonatology has pushed ever earlier the age at which a premature infant may be born without serious complications. Improvements in surgery and imaging have substantially reduced morbidity and mortality from a number of neonatal surgical conditions, especially congenital heart defects.

In chapter one, we discussed the history of neonatology. It began not as a sub-specialty of pediatrics, rather as a branch of obstetrics. In fact, the first neonatologists were obstetricians and neonatologists. We also discussed the scope of the problems covered by neonatology. Specifically, we talked about aspects of the epidemiology of prematurity and problems that fall under the purview of neonatology.

In chapter two, we dealt with the broad topic of perinatal medicine. As its name implies, perinatal medicine deals with the patient both before and after birth. Indeed, the problems related to newborn health are intricately tied to problems of maternal health. Therefore, we discussed issues related to prenatal care, specifically prenatal screening. We discussed some aspects of fetal medicine, including fetal surgery, indicating that more such procedures will be likely in the future. We discussed maternal medical conditions that impact on the fetus. For those participants who do not plan careers in neonatology, the most important maternal condition to remember is gestational diabetes.

We discussed intrauterine growth restriction, a problem a significant as fetal macrosomia that occurs in gestational diabetes. It turns out that many, if not most of the maternal conditions discussed in this course may result in intrauterine growth restriction.

Of the causes of intrauterine growth restriction, one of the classic, non-pathological causes is multiple gestation. We discussed how this phenomenon is becoming more common in recent years with the wider adoption of assistive reproductive technologies. Multiple gestations are also a major cause of preterm delivery, another recurring theme throughout this course.

In chapter two, we also touched briefly on preterm delivery, focusing on the major causes. We then discussed the broader topic of birth defects. The topic of birth defects became another recurring theme throughout the course. It is important to remember the distinctions between

malformations, dysplasias, deformations, and disruptions. Understanding these distinctions helps clarify concepts that bear on the entire science of pediatrics.

Chapter two then turned to issues concerning the effects of maternal drug use on the developing fetus. These effects do not respect whether the drug is legal or prohibited. As we learned, a number of legally prescribed drugs have adverse effects on fetal development.

A minor theme that appeared in many places in the course was the issue of maternal infections. These infections may impact fetal development and become important causes of fetal sepsis. In general practice, obstetrics, and pediatrics, general knowledge of maternal infections and their management will be important for the practitioner. Via a concept called “vertical transmission”, maternal infections often become congenital infections. Of these, HIV is the most important for the obvious reasons of long term effects on the health and life-span of the child.

In chapter three, the focus was on infant delivery. Here is where we encountered for the first time some of the complicated physiology of the birth process. Of these processes, the changes in the heart and the great vessels are of primary importance. In chapter three we also encountered the next recurring theme in the course. This was the physiology of the ductus arteriosus. The consequences of the ductus closing or failing to close depend on the particular physiological situation in the newborn. We returned to this question frequently throughout the course.

Chapter three then turned to issues related to maternal anesthesia and its effects on the neonate. Much of modern obstetrical anesthesia was designed with mindfulness toward protection of the neonate, while providing adequate anesthesia for the mother.

We then turned to another minor theme of the course, the process of resuscitation. The principles of resuscitation are the same as in any branch of medicine. Airway, breathing and circulation comprise the mnemonic device, The A, B, C's, that all physicians remember. The exception is the resuscitation of the infant suspected of having a congenital diaphragmatic hernia. In these cases, the resuscitation team should drop an oral-gastric tube and aspirate air before attempting to assist breathing with positive pressure.

After a brief discussion of the important signs in post-resuscitation care, chapter three turned the unpleasant topic of hypoxic-ischemic encephalopathy. Prevention of hypoxic-ischemic encephalopathy remains a major problem for obstetrics and neonatology. Prevention remains the mainstay because treatment is unavailable. Closely related to the topic of hypoxic-ischemic encephalopathy is birth trauma, which is a frequent cause of brain injury.

Birth trauma intersects with the issue of gestational diabetes because large babies are often injured during the process of birth. Recognizing and treating birth trauma is important, but prevention is also an active area of research.

The last topic covered in chapter three was infant transport. This is a special category of patient transport. Among the special features that are important to remember, the fact that newborn

transport teams carry prostaglandin illuminates the importance of understanding the physiology of the ductus arteriosus.

Chapter four dealt entirely with the normal infant. We covered routine care and the routine examination of the newborn in some detail. The important takeaway message from routine care was that parents should understand that they do not need to do the same things that hospital nurses do. Regarding the newborn examination, the key takeaway is that the pediatrician and nurses are screening for birth anomalies that require early intervention and correction.

Chapter four then turned to the related issues of support for parents and infant feeding. One of the largest sources of stress in the newborn period is infant feeding. This is an area where neonatology can offer insights to help parents adjust to caring for and feeding a newborn.

In this regard, chapter four's discussion of minor abnormalities was a useful section. A number of things occur during the first several days of life that may alarm new parents. It is important to anticipate these normal events and to explain them patiently to parents when they occur.

Neonatologists and hospital staff are well-tuned to anticipate and attend to common problems that occur in term infants. Chapter four dealt with these next. Here is another area where a well-informed caregiver can provide valuable advice and reassurance to a parent.

Finally, chapter four ended with a discussion of the care of the infant of a substance-abusing mother. This is actually a very delicate area of medicine, where the clinician must balance the demands of several constituencies: the mother, the baby, and the state.

Chapter five focused exclusively on care of the sick newborn. Here we encountered a detailed description of the newborn intensive care unit, or NICU. We discussed the design of NICUs down to the engineering of the lighting and the alarms. All of these were created with the developmental needs of the sensitive neonate.

In chapter five we touched again upon another sub-theme that recurred throughout the course. This concerns the three things that a newborn must be able to do before going home. Broadly speaking, this issue has to do with a concept called "hospital level of care". When a baby no longer requires care that can only be delivered in a hospital, they may safely go home. As a reminder, these are: breathe on their own, eat on their own, and regulate their body temperature.

This is a compelling concept because there is no longer a bright-line distinction between care that can only be delivered in a hospital and those that can be delivered at home. For example, parents can be taught to administer tube feedings for babies that require extra calorie support but otherwise do not need to be in a hospital. The benefits of these hospital-to-home transitions are that the stress on the baby and parents may be substantially reduced at home, and she might actually feed and grow better there than in the NICU.

Chapter six spent a fair amount of time discussing lung problems. This is because lung problems occupy a great deal of time and attention in neonatology. Of particular concern in chapter six was the care of premature lungs, in which inadequate surfactant is made to support adequate ventilation. In addition, the very support given gives rise to a number of untoward effects. Among these are bronchopulmonary dysplasia and the retinopathy of prematurity.

The control of breathing was also discussed in chapter six, particularly as it relates to apneas and bradycardias. Breathing on ones' own includes remembering to breathe. Therefore, a newborn probably should remain in the hospital if the respiratory center in the brain is not mature enough to respond to changes in arterial blood gas levels.

Chapter six also included a section on gastrointestinal problems of preterm infants. Of these, the most important one to remember is necrotizing enterocolitis. Just as hypoxic-ischemic encephalopathy remains an active subject of study, so is necrotizing enterocolitis. The causes are not completely known, apart from the fact that it is more common in prematures of earlier gestational age. It is not even clear if necrotizing enterocolitis is primarily an infectious or an inflammatory process.

In chapter six, the brain in the preterm infant was discussed, particularly the bleeding events that unfortunately occur. Identification and understanding of intraventricular hemorrhage and periventricular leukomalacia will help understand these entities. Hopefully this knowledge will contribute to their prevention and treatment as well.

Chapter six also returned to one of our recurring themes, the patent ductus arteriosus. In particular, we discussed the medical and surgical treatment of the entity. We also discussed neonatal infections.

Neonatal jaundice was a major area of discussion in chapter six. As opposed to some other neonatal problems about which little is known, quite a bit is understood about jaundice. We discussed the differential diagnosis of neonatal hyperbilirubinemia. We also discussed the various diagnostic and treatment modalities associated with each cause.

In similar fashion, much is known about the causes of anemia. We discussed at some length the differential diagnosis of anemia in the newborn. Broadly speaking, anemia can occur from too little production of red blood cells, too much loss/destruction of red blood cells, or sequestration of red blood cells. Fortunately, in neonatology, sequestration (as in the spleen) occurs rarely.

Finally, chapter six covered the problem of osteopenia of prematurity and ran a brief overview of outcomes for premature infants. Regarding the latter, chapter six taught that these outcomes keep changing for the better. Premature infants born in the twenty-first century have a much better chance of good long-term survival than prematures born in the twentieth century. The milestone of twenty-three weeks gestation appears to be a difficult one to reach. Successful care for neonates born before this date may require another major breakthrough in neonatology.

Chapter seven was devoted to neonatal problems. In this chapter, we dealt with primarily the problems of full-term infants that require NICU care. We discussed the broad differential

diagnosis of respiratory distress in the full-term newborn. We discussed some general features of diagnosis and some broad outlines regarding their treatments.

Chapter seven also dealt with upper airway disorders and anomalies. Here, as in other places in the course, knowledge of some congenital malformations is necessary. One entity, subglottic stenosis, is primarily an iatrogenic problem, caused by tracheal intubation.

Neonatal jaundice and infections were also discussed in this chapter. Chapter seven also covered the infant of the diabetic mother in greater detail. Issues related to hyper- or hypoglycemia in the newborn are usually handled by the neonatologist and are not seen in general practice. Therefore, it is important to have a general understanding of the biology, as covered in chapter seven.

Disorders of the gastrointestinal tract in the full-term newborn were next discussed in chapter seven. Of these, one important entity to remember was congenital diaphragmatic hernia. Another was intestinal malrotation with midgut volvulus. It turns out that milder forms of both these entities can present in later childhood or, rarely, adulthood. Therefore, caregivers from various disciplines should be aware of these entities and their pathophysiologies.

Chapter seven also covered a number of cardiac disorders. The development of the mammalian four-chambered heart is extremely complex. It is no surprise, therefore, that there are many respects in which the process can go wrong. We discussed the various classes of complex congenital heart disease. As expected, the recurring theme of the patent ductus arteriosus come

up here in a substantial way. Chapter seven discussed the way that these disorders are diagnosed and their various treatments.

The closely-related topics of renal and urogenital problems were covered next by chapter seven. Once again, the importance of understanding the differences among congenital anomalies became important. For example, congenital ureteropelvic junction obstruction is a malformation. Potter's sequence involves malformations and deformations. The malformation is renal agenesis. The deformation is the pulmonary hypoplasia, club feet, and abnormal facies that result from oligohydramnios.

Chapter seven also covered some topics in disordered development of sexual characteristics. It is the complexities of hormonal regulation that make these entities difficult to understand and diagnose. A helpful way to learn this section of chapter seven is to begin from the genetic sex of the individual. From there, understand the changes that occur during development and puberty.

In chapter seven we also covered several skin disorders that occur during the newborn period. The key takeaway from this section was that there is an inverse correlation between the appearance of the skin problem and its seriousness. The same goes for the names of these entities. Neonatal skin problems look awful and have awful names but almost all completely benign. Best of all, these conditions disappear spontaneously without treatment.

The sub-theme of hypoxic-ischemic encephalopathy appeared again in the discussion of neonatal seizures. Unfortunately, damage to neurons creates foci for seizure activity. Chapter seven dealt

with some of the more benign forms of seizures as well as some of the more serious ones. Just as pediatric and adult neurology are developing sciences, so is the case with neonatal neurology. More is being learned all the time about the developing brain, and the subject remains a focus of intense research.

Remaining with the brain, chapter seven delved into the topic of neural tube disorders. The topic was first broached in chapter two, when it was mentioned that folic acid supplementation reduces the incidence of neural tube disorders. The mechanism is not fully understood, but it is a simple and elegant preventive treatment.

The major forms of neural tube defects covered by chapter seven were spina bifida and anencephaly. Each entity results from failure of the embryonic neural tube to close at the caudal and rostral ends, respectively. Later in the chapter, we dealt with hypotonia in the newborn, a special case of neurological as well as muscular anomaly. Similar special cases are the special senses, hearing and vision, both of which were dealt with in chapter seven.

Chapter seven briefly entered the circulatory system again for a discussion of anemia and its opposite, polycythemia. We also discussed disorders of neutrophils, or white cells, and thrombotic disorders. Coagulation, or clotting disorders are thankfully rare in newborns, but chapter seven nevertheless dealt with these.

Finally, chapter seven covered the bone and joint disorders that are important in neonatology.

Chapter eight covered some special topics that are particular to management of patients in the neonatal intensive care unit. We discussed the topic of neonatal pain, and how it has evolved over the years. Chapter eight also discussed particular issues related to pharmacology, or the dosing of drugs in the neonatal intensive care unit.

A major concern of chapter eight was quality improvement and adverse events reporting. The study of harms is a relative latecomer in medicine in general. However, since the early days of neonatology, the imperative to do no harm has been central to the endeavor. Therefore, it is not surprising that neonatal intensive care units have robust and comprehensive systems in place to record adverse events. The purpose of the entire exercise is to devise ways to deliver the best care while doing the least harm.

For the same reasons, as discussed in chapter eight, evidence-based medicine has found a home in the neonatal intensive care unit. Nevertheless, a great deal remains to be discovered. The important takeaway from the section on evidence-based medicine was that more is unknown than is known. Much care and treatment in the neonatal intensive care unit, and elsewhere, is based on consensus opinion and empirical experience. While important, there remains a need to boost efforts to broaden the evidence base in neonatology.

In light of these important issues, chapter eight covered ethics issues in the neonatal intensive care unit. We discussed research ethics and the acquisition of informed consent.

A wise man once said that all therapy ultimately fails. In pediatrics, this is less true than in other specialties. Unfortunately, in the neonatal intensive care unit, some babies are not saved. Therefore, chapter eight dealt with issues surrounding palliative care and death in the neonatal intensive care unit.

We turned immediately to happier topics, particularly discharge and follow-up. More infants go home health from neonatal intensive care units than ever before. With improvements in technology, research, and evidence-based medicine, the trends continue to improve. But while these improvements are important and necessary, it is arguably the case that the most desirable outcome for neonatology is that it would put itself out of business. That is to say, the goal of the specialty should be to abolish premature birth, and to prevent and treat common congenital anomalies. Then, perhaps the care of the neonate may return to the inventors of neonatology, the obstetricians.

Course Questions and Answers

1. Who were the first neonatologists?
    a. Pediatricians
    b. Internists

c. Obstetricians

d. Anesthesiologists

Answer c. Neonatology arose as a subspecialty of obstetrics. It only later became a subspecialty of pediatrics.

2. What percent of total infant mortality is accounted for by prematurity?

    a. Fifty-five percent

    b. Sixty-five percent

    c. Seventy-five percent

    d. Eighty percent

Answer c

3. What percent of babies in the United States are born prematurely?

    a. Twelve-point five percent

    b. Fifteen percent

    c. Twenty percent

    d. Twenty-five percent

Answer a.

4. What is the most common cause of premature birth?

    a. Maternal infection

    b. Maternal illness

    c. Ascending infection

    d. Idiopathic

Answer d. Over half of premature births occur for no known reason. One third occur because of premature rupture of membranes. The remainder occur because of medical problems in the mother or the birth was induced electively.

5. Which region has the highest incidence of preterm birth?
    a. Northern Africa
    b. Western Africa
    c. Eastern Africa
    d. Southern Africa

Answer d. With almost eighteen percent preterm births, Southern Africa has the highest rates in the world, according to the World Health Organization

6. All of the following are reasons for mothers avoiding prenatal care except.
    a. Denial
    b. Incarceration
    c. Cost
    d. Substance abuse

Answer b. Even women in prison receive prenatal care

7. All of the following are performed routinely during prenatal exams except:
    a. Ultrasounds
    b. Blood tests
    c. X-rays

d. Urine tests

Answer c. Obstetricians want to expose the developing fetus to as little ionizing radiation as possible. For this reason, CT and fluoroscopy are also avoided.

8. All of the following maternal conditions are screened for at prenatal visits, except:
    a. HIV
    b. Tetanus
    c. Diabetes mellitus
    d. Rubella

Answer b. Tetanus is not communicable

9. What does human chorionic gonadotropin a test for?
    a. The progress of the pregnancy
    b. Neural tube defects
    c. Congenital developmental anomalies
    d. Congenital infections

Answer a. The level of human chorionic gonadotropin is measured against the predicted weeks of pregnancy to see if the fetus is growing as expected.

10. Mothers with cancer can be treated with anti-metabolic drugs in all stages of pregnancy except:
    a. The first trimester
    b. The second trimester
    c. The third trimester

d. At term

Answer a. The first trimester is when fetal organogenesis takes place. Anti-metabolic drugs interfere with this process. The mother may begin or resume cancer chemotherapy in the second trimester.

11. All of the following are common causes of intrauterine growth restriction except:

a. Maternal drug use

b. Beckwith-Wiedemann syndrome

c. Cytomegalovirus

d. Multiple gestation

Answer b. Beckwith-Wiedemann syndrome is usually a cause of macrosomia, not macrosomia.

12. All of the following are maternal risk factors for preterm delivery except:

a. Diabetes

b. Myasthenia gravis

c. Obesity

d. Underweight

Answer b. Obesity and underweight are both risk factors for preterm birth. Myasthenia gravis affects the newborn but does not affect birth weight.

13. Which of the following is a dysplasia?

a. The tetralogy of Fallot

b. Talipes equinus

c. Periventricular leukomalacia

d. Agenesis of the corpus callosum

Answer d. The tetralogy of Fallot is a malformation. Talipes equinus, or club foot, may be a deformation or a malformation. Periventricular leukomalacia is a post-natal event.

14. Which skin medicines are associated with birth defects

a. Isotretinoin

b. Erythromycin

c. Benzoyl peroxide

d. Isopropyl alcohol

Answer a. Women of childbearing age are warned to avoid using isotretinoin for acne treatment.

15. What is the most common way to acquire Toxoplasma?

a. From raw meat

b. From a dog

c. From a cat

d. From a rabbit

Answer c. Most mothers who acquire Toxoplasma do so from their own cat.

16. All of the following stimulate a baby's first breath except:

a. A finger in the baby's mouth

b. Room air

c. Passage through the birth canal

d. Handling by the obstetrician

Answer a. This method is used to keep the baby from taking a first breath when meconium aspiration is suspected.

17. At birth, Ohm's law predicts that the following happens to the pulmonary circulation:

a. The resistance decreases and flow increases
b. The resistance increases and flow increases
c. The resistance drops and flow decreases
d. The resistance increases and flow decreases

Answer a. Ohm's law states that flow is inversely related to resistance. At birth, pulmonary bed resistance decreases, and pulmonary blood flow increases.

18. All the following are measured in the Apgar score except:

a. Color
b. Pulse
c. Blood Pressure
d. Activity

Answer c. The other factors are respirations and irritability. Blood pressure is not part of the scale.

19. All of the following are initial steps of resuscitation except:

a. Pulse oximetry
b. Heart rate monitoring

c. Respiration monitoring

d. Warming

Answer a. Pulse oximetry is not part of neonatal resuscitation. All the other steps are done in the first moments after birth.

20. Which of the following is a criterion for diagnosing birth asphyxia?

a. Apgar score less than seven

b. Oxygen saturation less than ninety-five percent

c. Acidosis

d. Substantial malformations

Answer c. Apgar score less than three for longer than five minutes are associated with birth asphyxia. Oxygen saturations less than ninety-five percent may indicate hypoxia, but not necessarily birth asphyxia. Malformations do not predict birth asphyxia.

21. What is the most common birth trauma?

a. Caput succedaneum

b. Brachial plexus injuries

c. Cranial nerve injuries

d. Laryngeal nerve injuries

Answer a. Bruising on the head is by far the most common. Not on the list, but also common, is broken clavicle

22. All of the following are performed in the birthing suite except:

a. Erythromycin in the eyes

b. Vitamin K intramuscular injection

c. Umbilical disinfection

d. Infant warming

Answer c. No disinfection is currently performed for umbilical cord care

23. Which of the following vital signs is routine in the newborn nursery?

a. Heart rate

b. Blood pressure

c. Oxygen saturation

d. Urine output

Answer a. The others are measured, but not routinely, only if ordered by the physician for a newborn suspected of having a problem

24. Which of the following screening tests are done routinely in the well-baby nursery?

a. Vision screen

b. Hearing screen

c. Car seat test

d. Oxygen saturation

Answer b. There is no vision screening performed. The car seat test is only done for premature infants. Pulse oximetry is reserved for babies in whom some abnormality is suspected.

25. Which of the following diseases is the most common recessive genetic disease in Caucasians?

    a. Congenital hypothyroidism
    b. Phenylketonuria
    c. Cystic fibrosis
    d. Myasthenia gravis

Answer c. None of the others are known to be genetic diseases.

26. What disease is screened for during the newborn eye exam?

    a. Retinoblastoma
    b. Neuroblastoma
    c. Glioblastoma
    d. Astrocytoma

Answer a. The others do not appear in the eye. Congenital retinoblastoma appears as a white reflection instead of the normal red reflex

27. What is the most common heart murmur detected in the hours of life?

    a. Mitral valve prolapse
    b. Ventricular septal defect
    c. Patent ductus arteriosus
    d. Atrial septal defect.

Answer c. The ductal murmur usually disappears after about four hours. Mitral valve prolapse murmurs are the most common murmurs in young women. Ventricular septal defects are the

most common congenital defects, but not the most common source of murmurs. Atrial septal defect murmurs are rarer still.

28. In a very dark-skinned baby, where is the best location to identify jaundice?

    a. The sclera
    b. The gums
    c. The palms or soles
    d. The fingertips

Answer b. The gum line is the most sensitive site for detecting jaundice in a dark-skinned baby

29. The tongue is examined for what disorder?

    a. Tongue-tie
    b. Microglossia
    c. Thrush
    d. Geographic tongue

Answer a. Microglossia, or small tongue, is vanishingly rare. Thrush occurs, but generally not during the first twenty-four hours of life. Geographic tongue is a normal variant, usually not seen in newborns.

30. What normal finding affecting the sternum should be explained to parents?

    a. Prominent xiphoid process
    b. Prominent manubrium
    c. Prominent costo-sternal borders

d. Prominent claviculo-sternal joint

Answer a. The prominent xiphoid can appear as an abdominal mass that can be alarming to parents. It is perfectly normal.

31. Which of the following vaginal finding is abnormal?

a. Bloody secretions
b. Hypertrophic vaginal tissue
c. Hypertrophic clitoris
d. Whitish secretions

Answer c. Hypertrophic clitoris may be a sign of congenital adrenal hyperplasia and other disorders of sex development.

32. Which of the following is a normal finding in the male genitalia?

a. Chordee
b. Hypospadias
c. Hyperspadias
d. Redundant prepuce

Answer d. Redundant prepuce is foreskin. This is normal. The others are abnormal findings that require a urological consult.

33. Which part of the newborn exam should be performed every day?

a. The hip exam
b. The eye exam

c. The gag reflex exam

d. The Moro reflex exam

Answer a. The hip exam should be repeated at every opportunity until the patient is so large that the examiner cannot hold the knee and reach the greater trochanter. The other parts of the exam are bothersome to the newborn and need only be performed once.

34. What is the recommended sleeping position for newborns?

a. Supine on a flat surface

b. Supine on an angled surface

c. On the side on a flat surface

d. On the side on an angled surface

Answer a. The other positions are less safe but are not absolutely contraindicated as is prone sleeping. Angled positions are used for babies with symptomatic gastroesophageal reflux.

35. What is the first step for treating symptomatic reflux in newborns?

a. Shorter, more frequent feeds

b. Thickening feeds.

c. Angling the body up thirty degrees

d. Formula switch

Answer c. Some experts recommend shorter more frequent feeds, but this does not always solve the problem of an incompetent gastroesophageal sphincter. In addition, babies strongly dislike being denied milk when they are hungry.

36. All of the following are indications for NICU admission except:

a. Hypoglycemia
b. Macrosomia
c. Prematurity
d. Perinatal depression

Answer b. Large babies may be monitored for the presence of transient hypoglycemia, but they do not need to be admitted to the NICU to do so.

37. Which of the following is not necessary before transporting a sick newborn to a NICU?

a. Venous access
b. Airway control
c. Effective respirations
d. Effective peripheral circulation

Answer a. If venous lines cannot be placed, medications can be given intramuscularly, via endotracheal tube, or intraosseously. The other answers are part of the airway, breathing, circulation mantra.

38. To be fed by mouth a baby must:

a. Have a coordinated pyloric reflex
b. Have a coordinated grasp and suck reflex
c. Have a coordinated suck and swallow reflex
d. Have a gag reflex

Answer c. Gag reflexes are important, but some babies do not have one. The other reflexes are not relevant.

39. Which gastrointestinal problem is associated with prematurity?
    a. Hirschsprung's disease
    b. Necrotizing enterocolitis
    c. Pyloric stenosis
    d. Tracheoesophageal sphincter

Answer b. The others are not associated with prematurity.

40. What medication is given to mothers to accelerate the production of fetal surfactant during preterm labor?
    a. Hydrocortisone
    b. Fluticasone
    c. Betamethasone
    d. Cortisol

Answer c. The others are steroids, but they are not tested or used for the purpose put forth in the question.

41. How is respiratory distress syndrome differentiated from transient tachypnea of the newborn?
    a. Respiratory distress syndrome generally resolves in six hours
    b. Transient tachypnea of the newborn is treated with surfactant therapy

c. Respiratory distress syndrome is characterized by ground glass opacities on chest x-ray

d. Transient tachypnea of the newborn is characterized by patchy infiltrates on chest x-ray

Answer c. Respiratory distress syndrome results from surfactant deficiency. Transient tachypnea of the newborn results from retained lung fluid. Its x-ray appearance is of diffuse streaky opacities, not patchy infiltrates, as would be seen in pneumonia.

42. All the following are diagnostic criteria for bronchopulmonary dysplasia except:

a. Baby has streaky opacities on chest x-ray

b. Baby needs supplemental oxygen for longer than twenty-eight days

c. Respiratory distress develops when respiratory assistance is weaned

d. Baby needs positive pressure ventilation for at least the first two weeks

Answer a. The classic x-ray pattern is diffuse hyperinflation with cystic changes. Streaky opacities are characteristic of transient tachypnea of the newborn.

43. What is the most common brain injury in premature infants?

a. Periventricular leukomalacia

b. Hydrocephalus

c. Intraventricular hemorrhage

d. Agenesis of the corpus callosum

Answer c. Bleeds in the germinal matrix may be mild an asymptomatic. They are nevertheless common in premature infants.

44. What is the principal treatment of moderate to severe retinopathy of prematurity?

a. Decreasing oxygen delivery to the infant
b. Phototherapy
c. Laser ablation
d. Expectant management

Answer c. Phototherapy is reserved for the treatment of hyperbilirubinemia. Expectant management, or watchful waiting, is not recommended for severe retinopathy of prematurity.

45. The ductus arteriosus connects what two great vessels?

a. The aorta and the pulmonary artery
b. The aorta and the superior vena cava
c. The aorta and the inferior vena cava
d. The aorta and the pulmonary vein

Answer a. Prior to birth, blood in the right ventricle mostly bypasses the pulmonary circulation and enters the aorta through the ductus arteriosus

46. What is the final end stage result of failure of the ductus arteriosus to close?

a. Pulmonary hypertension
b. Pulmonary congestion
c. Pulmonary arteriovenous malformations
d. Congestive heart failure

Answer d. Pulmonary congestion and hypertension precede congestive heart failure.

47. What kind of lung disease does meconium aspiration syndrome cause?

a. Obstructive lung disease
b. Restrictive lung disease
c. Infectious lung disease
d. Developmental lung disease

Answer a. Restrictive lung disease refers to a small total lung capacity. The pneumonia of meconium aspiration syndrome is non-infectious

48. What is the most sensitive indicator of congenital pneumonia?

a. Ultrasound findings
b. X-ray findings
c. Oropharyngeal isolation of group B strep
d. Oropharyngeal isolation of *K. pneumoniae*

Answer b. X-ray is most sensitive. The other modalities are not useful for diagnosis.

49. Pulmonary edema is caused by all the following except:

a. Birth asphyxia
b. Respiratory distress syndrome
c. Bronchopulmonary dysplasia
d. Patent ductus arteriosus

Answer c. Bronchopulmonary dysplasia is characterized by hyperinflation and cystic changes on x-ray.

50. What is the definitive therapy for the most common cause of neonatal pulmonary hemorrhage?
    a. Prostaglandin
    b. Indomethacin
    c. Surfactant
    d. Surgical closure of the patent ductus arteriosus

Answer d. Indomethacin, a non-steroidal anti-inflammatory, may help close the ductus, but it inhibits clotting. Therefore, it is relatively contraindicated for treatment of the patent ductus. Surfactant has been used but is not definitive therapy. Prostaglandin keeps the ductus patent.

51. Which of the following is characterized by segments of lung formed that are not attached to the pulmonary arterial blood supply?
    a. Congenital lobar emphysema
    b. Congenital pulmonary sequestration
    c. Congenital cystic adenomatoid malformation
    d. Congenital diaphragmatic hernia

Answer b. Sequestrations often become infected and must be removed

52. Which of the following are characterized by entire lobes of a lung replaced by non-functional empty space?
    a. Congenital lobar emphysema
    b. Congenital pulmonary sequestration

c. Congenital cystic adenomatoid malformation

d. Congenital diaphragmatic hernia

Answer c. They generate the same physiological effects as lobar emphysema.

53. Which anomaly results from failure of a tube to divide in two?

a. Laryngeal web

b. Tracheoesophageal fistula

c. Pulmonary hypoplasia

d. Oligohydramnios

Answer b. The others are not the result of tube formation

54. All of the following may result in pulmonary hypoplasia except:

a. Potter syndrome

b. Oligohydramnios

c. Congenital diaphragmatic hernia

d. Tracheoesophageal fistula

Answer d. Potter syndrome causes oligohydramnios.

55. What is the first step in the work-up of choanal stenosis?

a. Swallowing study

b. Insertion of a nasogastric tube

c. X-ray

d. Ultrasound

Answer b. The object is not to reach the stomach with the tube, but only to assess whether the catheter can pass through the nose.

56. Which portion of the respiratory tract has the highest resistance to flow?

    a. The nose
    b. The epiglottis
    c. The trachea
    d. The carina

Answer a. Unfortunately, this is also the part of the respiratory tract that is most often blocked.

57. If a tube's diameter decreases by one half, by how much does resistance to flow increase?

    a. Two times
    b. Four times
    c. Eight times
    d. Ten times

Answer c. The resistance to flow in a tube varies as the radius raised to the third power. Therefore, cutting the diameter in half increases eight times, or two to the third power.

58. What is the physiological reason for upper airway collapse in laryngomalacia?

    a. The tube is too narrow
    b. The tube is too floppy
    c. The tube is too rigid
    d. a or b

Answer d. Airway collapse occurs according to Bernoulli's principle. The faster the air flow, the more the pressure drops. Floppy or narrow airways are more likely to collapse under these circumstances.

59. Which upper airway obstructive disease is iatrogenic?

    a. Laryngeal web
    b. Choanal stenosis
    c. Tracheoesophageal fistula
    d. Subglottic stenosis

Answer d. Subglottic stenosis most often occurs as a result of inflammatory damage from tracheal intubation.

60. In physics, what is compliance?

    a. Volume divided by pressure
    b. Flow divided by resistance
    c. Pressure divided by resistance
    d. Pressure divided by flow

Answer a. Flow divided by resistance has no physical meaning. Pressure divided by resistance gives flow. Pressure divided by flow gives resistance.

61. How is pneumothorax treated?

    a. Expectant management
    b. Needle aspiration

c. Chest tube and suction

d. All of the above

Answer d. The intervention depends on the size of the pneumothorax

62. What physiology causes tension pneumothorax?

a. Two-way valve physiology

b. Ball-valve physiology

c. Serial valve physiology

d. Parallel valve physiology

Answer b. Air enters through the chest wall defect with each respiration without exiting, causing expansion and compression of the space on the contralateral side.

63. How is tension pneumothorax treated?

a. Bag-mask ventilation

b. Nasogastric tube decompression

c. Thoracoscopy

d. Needle decompression

Answer d. The other interventions would not help and could make the situation worse.

64. What causes chylothorax?

a. Infection

b. Congenital malformation

c. Idiopathic

d. Arteriovenous malformation

Answer c. No one knows what causes naturally-occurring chylothorax. However, it can be caused by trauma or surgery

65. All the following are causes of pleural effusion except:

a. Congenital diaphragmatic hernia
b. Heart failure
c. Upper airway obstruction
d. Pneumonia

Answer a. Pneumonia causes leak syndromes that allows the influx of fluid and cells. Heart failure and upper airway obstruction cause effusions by changes in venous pressure.

66. Which of the following is a major class of hyperbilirubinemia?

a. Sickle cell type
b. Spherocytotic
c. Conjugated
d. Galactosemic

Answer c. The other is unconjugated hyperbilirubinemia

67. Conjugated hyperbilirubinemia results all the following except:

a. Hepatitis B
b. Galactosemia
c. Rh disease

d. Biliary atresia

Answer c. Rh disease is a cause of unconjugated hyperbilirubinemia

68. How is biliary atresia treated?

a. Surgery

b. Phototherapy

c. Stimulation of hepatic uptake of bilirubin

d. Exchange transfusion

Answer a. Phototherapy is a treatment for unconjugated hyperbilirubinemia. Exchange transfusion is used to reduce dangerously high levels of bilirubin to spare the brain from damage.

69. All the following are intrinsic causes of hemolysis except:

a. Red cell membrane conditions

b. Red cell enzyme conditions

c. Globin synthesis defects

d. Rh disease

Answer d. Rh disease is an extrinsic cause of hemolysis.

70. What type of cause of hemolysis is glucose-six-phosphate deficiency?

a. Red cell membrane condition

b. Red cell enzyme condition

c. Globin synthesis defect

d. Rh disease

Answer b. This enzyme in red blood cells causes hemolysis in the presence of certain drugs and toxins

71. Which type of hemolytic condition is Sickle cell disease?

    a. Red cell membrane condition
    b. Red cell enzyme condition
    c. Globin synthesis defect
    d. Rh disease

Answer c. In hypoxic conditions, sickle hemoglobin polymerizes in such a way that the polymers break, or lyse, the cell membrane.

72. What is the most common cause of extrinsic hemolysis?

    a. Red cell membrane condition
    b. Red cell enzyme condition
    c. Globin synthesis defect
    d. Rh disease

Answer d. The next most common is sepsis

73. What is the most common non-hemolytic cause of unconjugated hyperbilirubinemia?

    a. Breastfeeding jaundice
    b. Obstructive jaundice
    c. Enzyme deficiency jaundice
    d. Excessive production jaundice

Answer a. There is an enzyme in breast milk that inhibits hepatic uptake of bilirubin.

74. What is the inciting event in the development of congenital diaphragmatic hernia?

a. Intestinal malrotation
b. Mid-gut volvulus
c. Intestinal torsion
d. Failure of the diaphragmatic leaves to fuse

Answer d. The issue is timing. If the leaves of the diaphragm do not fuse prior to abdominal contents reentering the body cavity, the intestines could end up in the chest cavity.

75. What pulmonary problem is caused by congenital diaphragmatic hernia?

a. Pulmonary malformation
b. Pulmonary hypoplasia
c. Pulmonary disruption
d. Pulmonary deformation

Answer b. The lung tends to form incompletely because of the mass effect of intestines in the thorax.

76. All of the following are physical signs of congenital diaphragmatic hernia except:

a. Currant jelly stools
b. Bowel sounds in the chest
c. Point of maximum impact displaced to the right
d. X-ray evidence of loops of bowel in the chest.

Answer a. This is a sign of intestinal intussusception, a rare finding in neonates.

77. What is the initial step in stabilization of an infant with suspected congenital diaphragmatic hernia.

    a. Bag-mask ventilation
    b. Nasogastric catheter suction
    c. Establishment of venous access
    d. Airway clearance

Answer b. This must be done before the airway is secured. This is a violation of the airway – breathing- circulation sequence. However, it is necessary to avoid introducing air into the intestines, lest the remaining lung be compromised.

78. All of the following is true of pyloric stenosis but the following:

    a. It is more common in girls
    b. It results from hypertrophy of the muscular layer
    c. It is associated with projectile vomiting
    d. It is treated by myotomy of the pylorus

Answer a. Pyloric stenosis is more common in boys.

79. Which metabolic derangement is characteristic of pyloric stenosis?

    a. Metabolic acidosis
    b. Metabolic alkalosis
    c. Respiratory acidosis

d. Respiratory alkalosis

Answer b. The expulsion of large amounts of hydrochloric acid gives rise to metabolic alkalosis.

80. Intestinal malrotation is what type of congenital anomaly?

a. Malformation

b. Deformation

c. Dysplasia

d. Disruption

Answer a. Malrotation is a failure of the intestines to return to the abdominal cavity in such a way that the colon is fixed in place.

81. The following are all signs of mid-gut volvulus except:

a. Bowel sounds in the chest

b. Bilious vomiting

c. Distension

d. Shock

Answer a. This is a sign of congenital diaphragmatic hernia.

82. The following are all signs of Hirschsprung's disease except the following:

a. Toxic megacolon

b. Failure to pass the first meconium

c. Abdominal mass

d. Bilious vomiting

Answer d. This is a sign of obstruction distal to the ampulla of Vater. All the other signs are typical of Hirschsprung's disease.

83. All the following are bacteria responsible for neonatal sepsis except:

    a. *Streptococcus pneumoniae*
    b. Group B strep
    c. *Listeria monocytogenes*
    d. *Escherichia coli*

Answer a. This is the most common cause of sepsis in older children

84. What are the antibiotics used in combination to empirically treat neonatal sepsis?

    a. Ampicillin/clavulanate
    b. Ampicillin/gentamicin
    c. Amoxicillin/azithromycin
    d. Trimethoprim/sulfamethoxazole

Answer b. Gentamicin treats E. coli. Ampicillin covers Group B strep and Listeria.

85. What is the most important non-vertically transmitted virus of neonates?

    a. Respiratory syncytial virus
    b. Cytomegalovirus
    c. Herpes simplex virus
    d. Human immunodeficiency virus

Answer a. The others are all vertically transmitted

86. What is the primary complication of respiratory syncytial virus infection?

a. Pneumonia
b. Respiratory distress syndrome
c. Bronchiolitis
d. Bronchiectasis

Answer c. Respiratory syncytial virus can cause pneumonia, but this is far rarer than is bronchiolitis. Bronchiectasis is more common in chronic pulmonary infections associated with cystic fibrosis.

87. What is the most common fungal cause of neonatal infections?

a. Aspergillus
b. Candida
c. Histoplasma
d. Blastomyces

Answer b. Aspergillus occurs, but Candida is more common. Histoplasma and Blastomyces occur in older children and adults.

88. What is the mechanism of hypoglycemia in infants of diabetic mothers?

a. Pancreatic insufficiency
b. Hyperactive pancreatic beta cells
c. Hyper active pancreatic alpha cells

d. Pancreatic obstruction

Answer b. The fetus's pancreas works well, even if the mother's does not. This means that it produces adequate insulin. When abruptly separated from the source of glucose, the beta cells pumping out high quantities of insulin cause the infant to become hypoglycemic.

89. All of the following are classes of congenital heart defects except:

a. Hypoplastic

b. Obstructive

c. Restrictive

d. Cyanotic

Answer c. The fourth class is septal.

90. What is the most common congenital heart defect?

a. Ventricular septal defect

b. Atrial septal defect

c. Patent ductus arteriosus

d. Aortic stenosis

Answer a. The others are not nearly as common

91. All of the following are types of cyanotic heart disease except:

a. Tetralogy of Fallot

b. Total anomalous venous return

c. Transposition of the great arteries

d. Patent ductus arteriosus

Answer d. This is most often a cause of congestive heart disease

92. Bartter syndrome is characterized by

a. Hypokalemia
b. Hyponatremia
c. Hypotension
d. Hypothyroidism

Answer a. This rare inherited defect is characterized by low potassium levels and alkalosis. It is caused by a defect in the function of the kidney's filtering system.

93. What is the initial step in Potter's sequence?

a. Club foot
b. Bilateral renal agenesis
c. Oligohydramnios
d. Pulmonary hypoplasia

Answer b. The lack of urine production leads to low amniotic fluid, which leads to pulmonary hypoplasia and club feet (a deformation)

94. What are the effects of congenital adrenal hyperplasia?

a. Feminization of genetic males
b. Delayed puberty
c. Masculinization of genetic females

d. Delayed conversion of testosterone

Answer c. Congenital adrenal hyperplasia is caused by excessive androgen production by the adrenal glands

95. When does erythema toxicum neonatorum appear?

a. Two hours of life
b. Two days of life
c. Two weeks of life
d. Two months of life

Answer b. Erythema toxicum is seldom present at birth. At two weeks of life it is more likely to be neonatal acne

96. Neonatal cephalic pustulosis is also known as

a. Milia
b. Baby acne
c. Melanotic pustulosis
d. Histiocytosis

Answer b. Milia are punctate white spots usually on the nose. Melanotic pustulosis is present at birth. Histiocytosis is a serious condition that is very rare in neonates.

97. When do benign newborn seizures typically begin?

a. Hours after birth
b. Before birth

c. Fifth day of life

d. There are no such things as benign seizures

Answer c. There are indeed such things as benign seizures. They occur around the fifth day of life. They resolve without treatment

98. What is haptoglobin useful for determining?

a. The cause of formula intolerance

b. The cause of anemia

c. The cause of hemolysis

d. The cause of bone marrow failure

Answer b. Hemolysis and bone marrow failure can give rise to anemia, but haptoglobin cannot determine their causes. However, haptoglobin can help determine the cause of anemia, particularly whether it is hemolytic or aplastic

99. What is the excess production of red blood cells called?

a. Hypercythemia

b. Plethora

c. Polycythemia

d. Hypererythrocytosis

Answer c. Plethora is the name of the red skin condition associated with polycythemia.